SYMPOSIUM ON DISEASES OF THE PANCREAS

Vol. 18 AUGUST, 1945 No. 2

SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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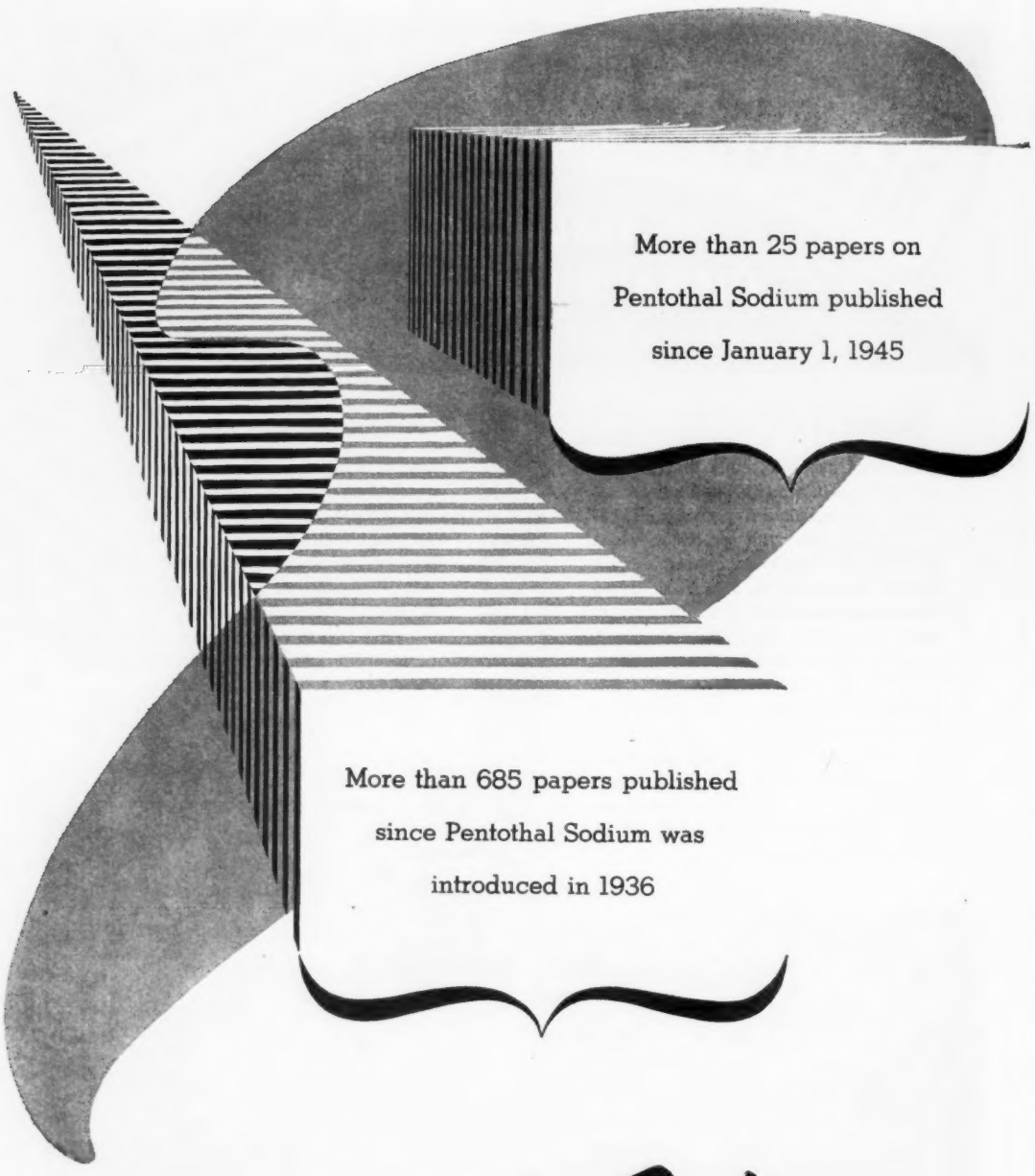
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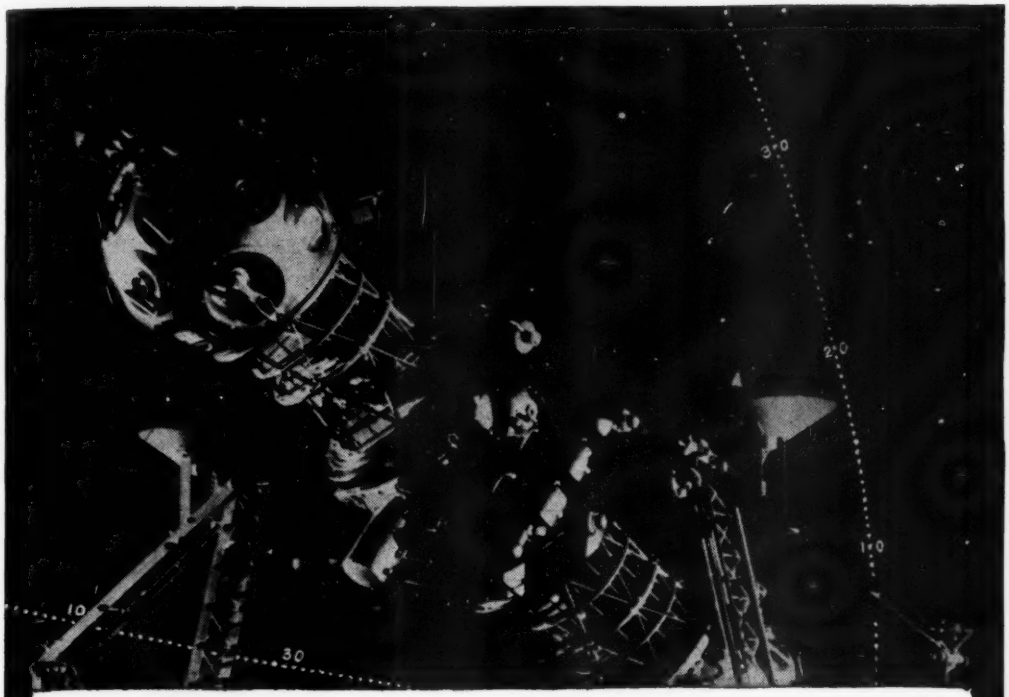

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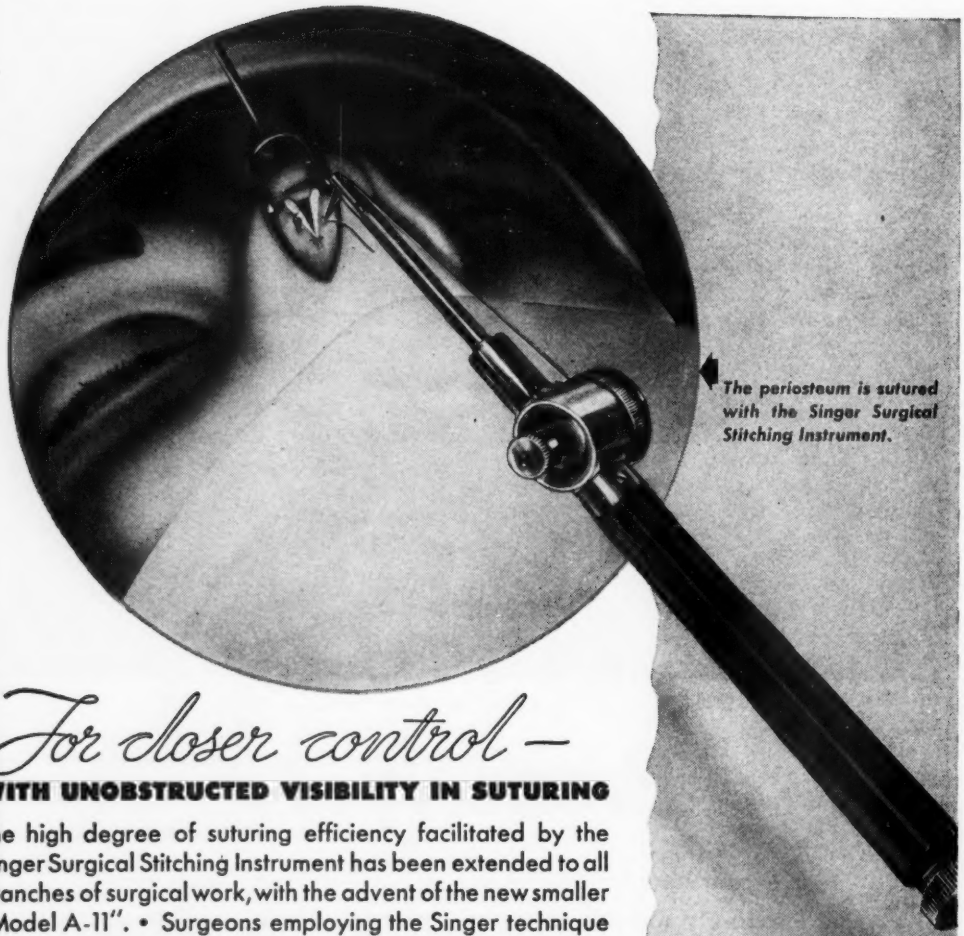

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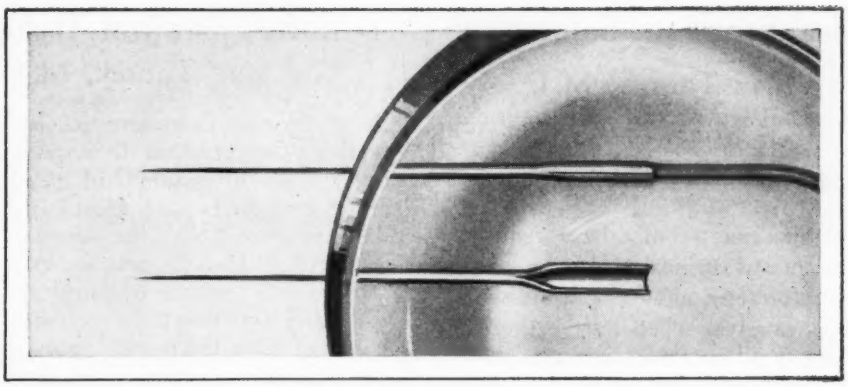

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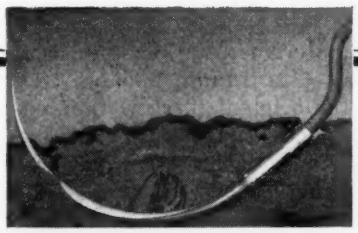

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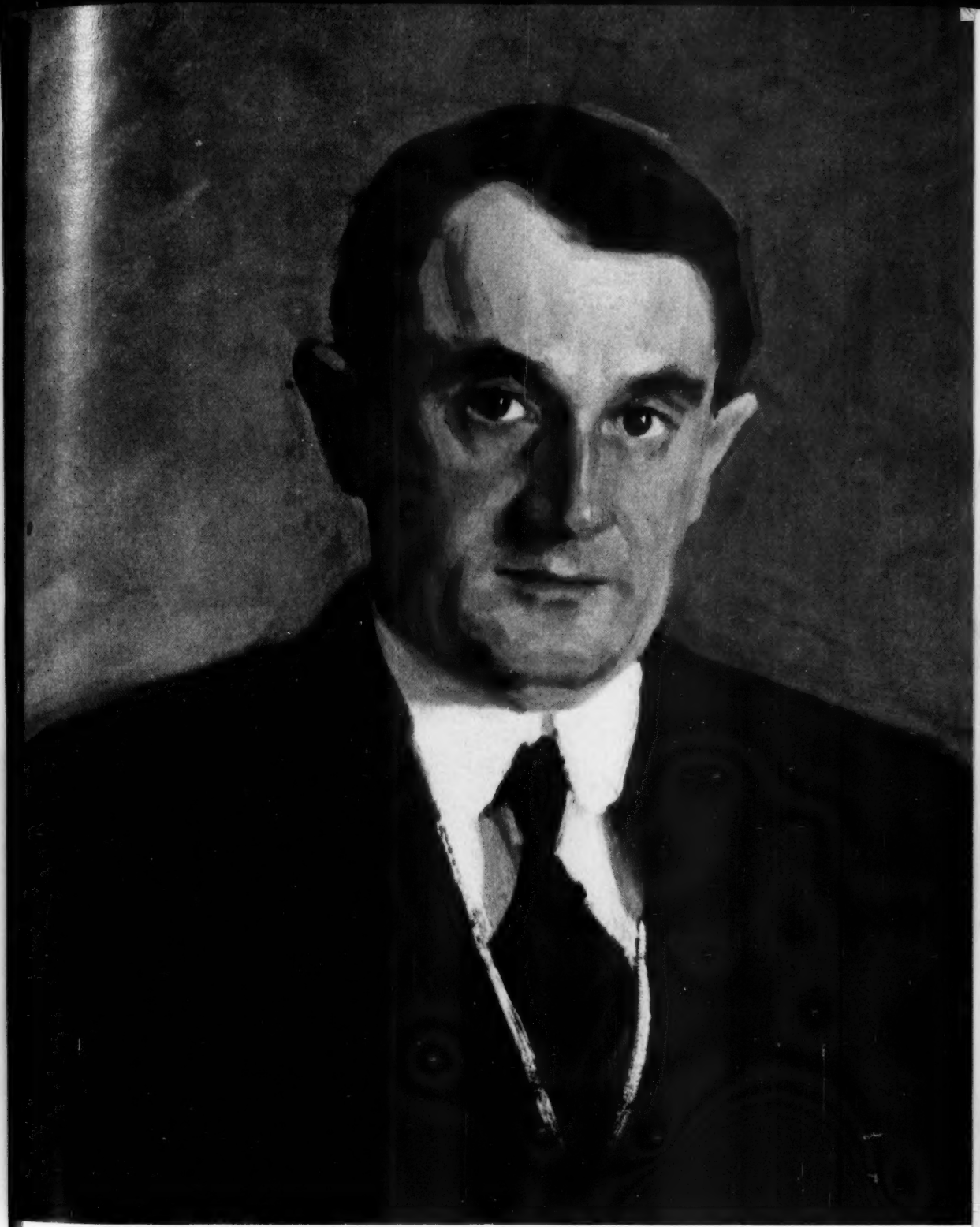

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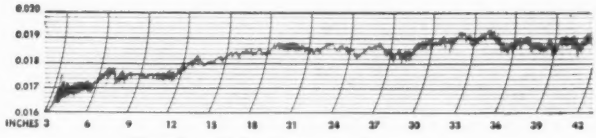

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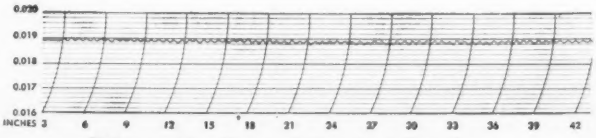

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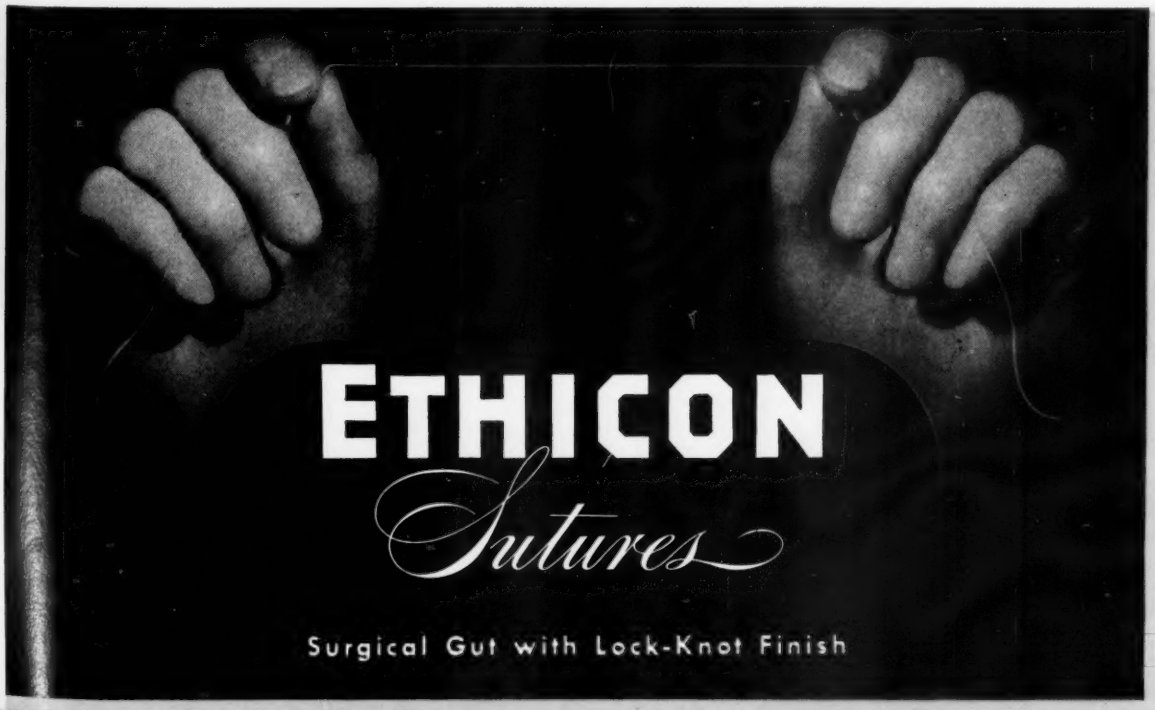

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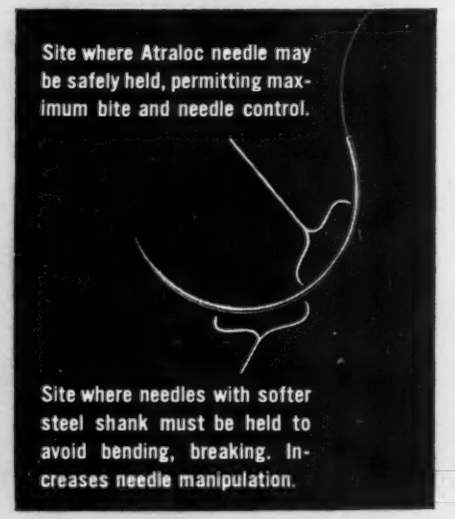
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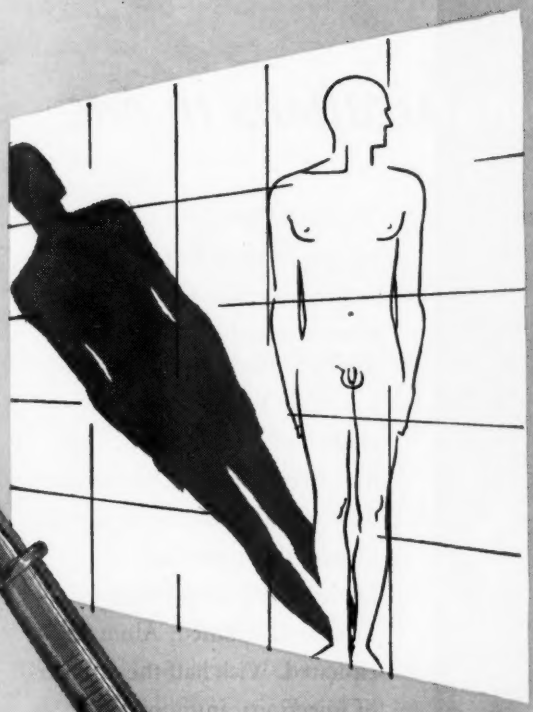

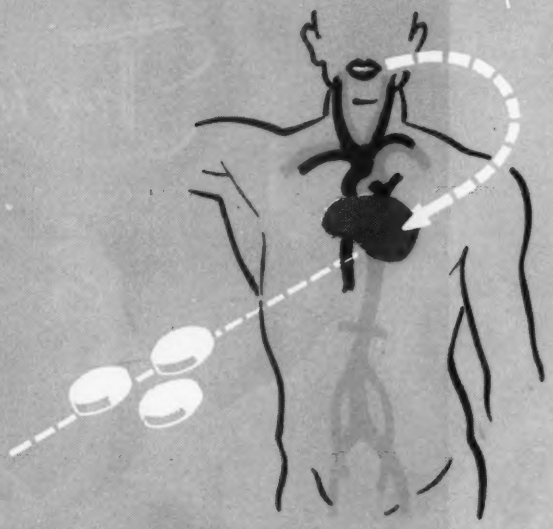

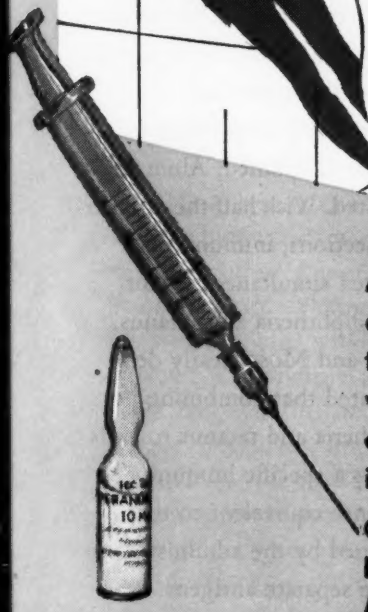

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SURGERY

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Symposium on Diseases of the Pancreas

RESECTION OF THE DUODENUM AND HEAD OF THE PANCREAS FOR PRIMARY CARCINOMA OF THE HEAD OF THE PANCREAS AND AMPULLA OF VATER

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THE original operation of resection of part of the duodenum and head of the pancreas for carcinoma of the ampulla of Vater, as reported by Whipple and associates[1] was modified a short time later by Brunschwig[2] to a more radical resection for carcinoma of the head of the pancreas. The technique presented by Brunschwig, which was devised for carcinoma of the head of the pancreas, makes the principle applicable to many more patients since carcinoma is much more frequent in the head of the pancreas than in the ampulla of Vater. With earlier diagnoses and improvements in preoperative treatment of the patient (including the tremendous value of ample transfusions on the operating table) more and more such operations will be performed. The operation is complicated and literally consumes hours for completion; for these reasons numerous modifications of the original operation reported by Whipple and associates have been suggested. Because of the large number already presented, we are apologetic for reporting another, but appreciation of maintenance of certain physiologic principles and efforts to shorten the numerous procedures of the operation have led us (through our very limited experience with five cases of resection) to development of a procedure which will be described in detail later.

An important modification (suggested by Whipple[1] in 1941) of the original operation is the anastomosis of the jejunum to the common duct, instead of to the gall bladder, to prevent the serious effects of infection (suppurative cholangitis) and a "blowout" at the ligated end of the common duct. As a matter of fact, the technique reported by Orr,[3] in 1941, on a patient who previously had had a cholecystectomy, utilized a choledochojejunostomy. A one-stage method reported in 1942 by Pearse,[4] consisting of the implantation of the cut end of the pylorus into the side of the jejunum, was a very simple one but the anatomosis of the jejunum to the gall bladder would appear undesirable.

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In 1941, Whipple[1] and Trimble and associates[5] independently reported a one-stage operation consisting of antecolic anastomosis of the jejunum to the end of the common duct and the pyloric end of the stomach (see Fig. 1). The anastomosis was made so that the food stream passed upward toward the lesser curvature of the stomach and over the transplanted end of the common duct. Hunt[6] (1941) performed the operation in one stage, transplanting the cut end of the pancreas into the open end of the distal duodenum or proximal jejunum. In 1942, Orr[7] reported a one-stage procedure in which he closed the pyloric end of the stomach, did a gastroenterostomy, and transplanted the common duct into

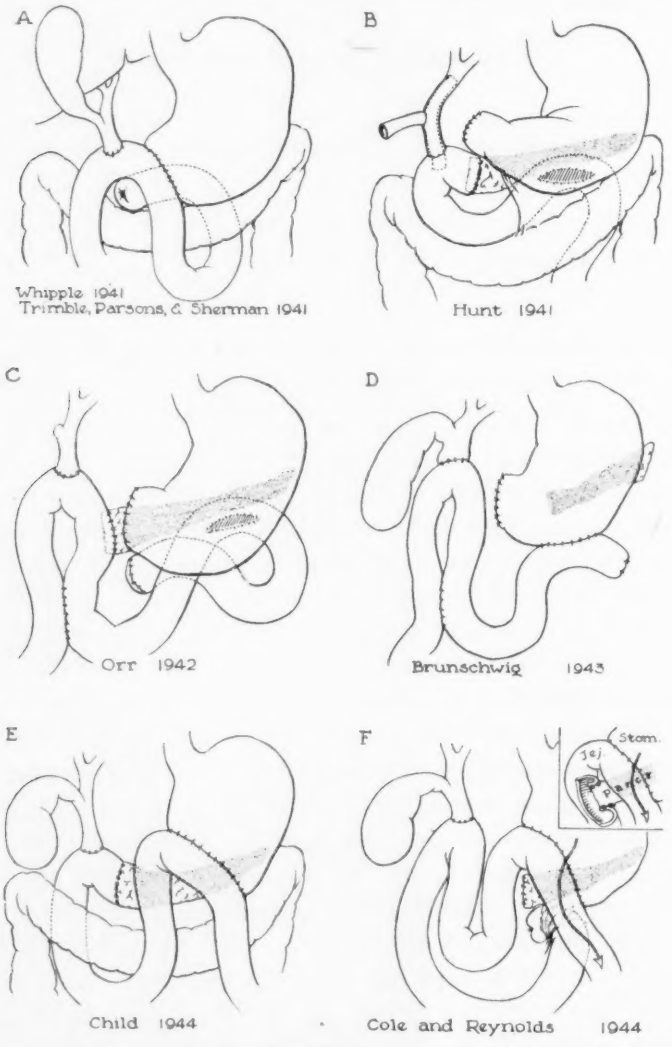

Fig. 1.—Numerous types of one-stage resections for carcinoma of the head of the pancreas or ampulla of Vater have been suggested. Among these are operations described by (*A*) Whipple and Trimble and associates, (*B*) Hunt, (*C*) Orr, (*D*) Brunschwig, (*E*) Child, and (*F*) Cole and Reynolds.

a loop of jejunum (see Fig. 1). The one-stage procedure reported by Brunschwig[8] (1943) consists of a posterior gastroenterostomy and anastomosis of a loop of jejunum to the common duct with a jejunojejunostomy performed between the two loops of jejunum (see Fig. 1). Along with several other methods, Child[9] reported a simplified one-stage procedure (1944) in which he implanted the cut end of the pancreas into the open end of the jejunum. The stump of common duct was transplanted into the jejunum proximal to the end-to-side gastrojejunostomy (see Fig. 1). Dennis[10] (1942) reported a one-stage resection

in which he performed a cholecystojejunostomy and a retrocolic Polya gastrojejunostomy. Cattell[11] (1944) described a technique in which he performed an end-to-end gastrojejunostomy according to a Billroth technique, transplanted the end of the common duct and cut end of the pancreas into a loop of jejunum.

The recent demonstration of the fact that we can operate for hours even on aged patients, if we resort to meticulous preoperative care and give large quantities of blood during the operation, now justifies performance of resections of the duodenum and head of the pancreas in one stage, with of course a few exceptions. For this reason, and for the sake of brevity, the discussion of the various modifications has been limited to one-stage procedures. If emergency indicates, any of the one-stage procedures can be broken into a two-stage operation of variable types.

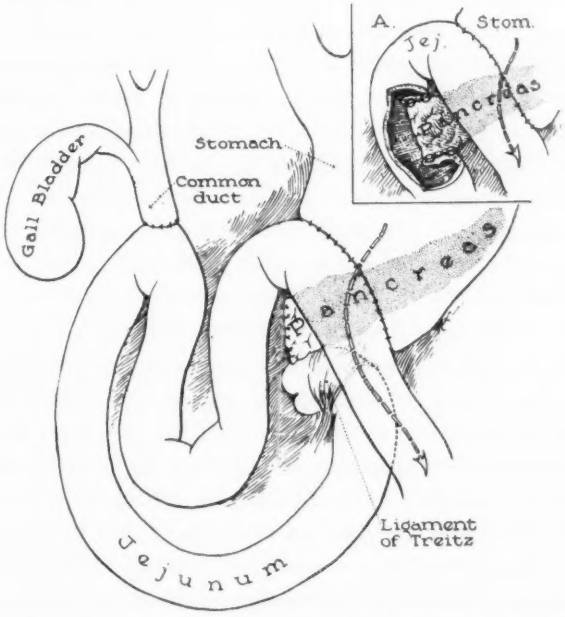

Fig. 2.—Technique of the one-stage resection of duodenum and head of the pancreas adopted by us after trial with several different types. Note that the common duct is transplanted proximal to the gastrojejunostomy so that the food stream will not pass over it but will pass downward (assisted by gravity) instead of upward and over the transplanted duct as in some operations recommended.

Insert shows an alternate procedure of also transplanting the cut end of the pancreas into the jejunum. The proximal loop of jejunum is left long to make room for transplantation of the common duct and, if desired, also the stump of pancreas; however, it need not be so long if transplantation of the stump of the pancreas into the jejunum is not done or contemplated.

TECHNIQUE OF OPERATION

In the five cases herein reported we have utilized several different types of operations. However, the method which we have finally adopted as the procedure of choice is one hitherto unreported and consists of a one-stage resection of the duodenum and head of the pancreas with transplantation of the common duct into the jejunum and performance of an end-to-side gastrojejunostomy (see Fig. 2) so that the food stream will not pass over the transplanted end of the common duct.

A longitudinal midline or modified transverse incision is made in the upper abdomen. After demonstrating that no metastases are present it must be determined whether or not the tumor can be dissected from the superior mesenteric and portal veins. To ascertain this, the peritoneum along the greater curvature of the duodenum is cut and the duodenum with the head of the pancreas lifted

up. We have found dissection easier if begun inferiorly and laterally, but if a line of cleavage is not found with one approach, another should be tried. Perhaps the most important precaution is not to injure the superior mesenteric or portal vein; an accidental tear can be repaired, but such an accident consumes precious time in its repair and for other reasons, including possible thrombosis, should be avoided if at all possible. The common duct is divided as far distally as possible. The gastroduodenal and inferior pancreaticoduodenal arteries are then ligated, but not until the operability of the tumor is definitely established, since ligation of both of these vessels would result in gangrene of the duodenum. The pylorus and distal duodenum at the ligament of Treitz are then divided (see Fig. 2). The distal end of the duodenum or proximal end of the jejunum is turned in with at least two rows of sutures, the outer of which should be cotton or silk. A long loop of jejunum (at least fifteen inches) is then brought up and an end-to-side gastrojejunostomy performed. The chief purpose of the long loop is to have room for transplantation of the stump of pancreas into this loop, if time permits and the procedure seems advisable. The end of the common duct is transplanted into the jejunum, leaving as much distance as possible between the site of transplantation and the gastrojejunostomy so that possible contamination or exposure to food stream can be minimized. In this anastomosis the mucosa of the jejunum should be anastomosed directly to the mucosal surface of the common duct (with interrupted fine catgut), to minimize stenosis, as has been emphasized by Cattell. A second row of interrupted silk or cotton, attaching serosa to serosa, is of course indicated.

The jejunal loop may be brought up either anterior or posterior to the colon depending upon the length of the jejunal mesentery and thickness of the mesocolon. If the jejunal mesentery is short and the jejunum brought up anterior to the colon, anastomosis of this loop of jejunum to the end of the common duct may put tension on the proposed suture line at the site of transplantation of the common duct; if this is the case an opening should be made in the mesocolon and the jejunal loop brought up posterior to the colon. If the edge of the opening in the mesocolon is attached to the walls of the two loops of jejunum by numerous interrupted sutures there need be no fear of development of intestinal obstruction. In Case 1, in which the technique as described and illustrated in Fig. 2 was followed, the jejunum was brought up anterior to the colon.

We have not been transplanting the cut end of the pancreas into the intestine largely because, to date, very little ill effect has been observed by the various authors reporting on this subject, following complete closure of the pancreatic stump. This problem will be discussed in greater detail later.

During closure of the wound it is advisable to insert a drain down to the stump of the pancreas, largely because a pancreatic fistula develops so commonly in spite of efforts to ligate the pancreatic duct, and close the stump of the pancreas with nonabsorbable sutures.

DISCUSSION OF OPERATIVE PRINCIPLES

In addition to efforts to shorten the operative procedure one must endeavor to restore anatomic structures in such a way that normal physiology will not be disturbed.

Unless the tumor has invaded the duodenum so far distally as to impinge upon the ligament of Treitz, we believe it is timesaving to transect the duodenum proximal to the ligament of Treitz and turn it in, rather than to cut the ligament itself and dissect the bowel from the mesenteric vessels. Invagination of a

stump of bowel the size of the duodenum can be done so rapidly and safely that it will not be time-consuming. It appears to us that anastomosis of the cut end of the stomach to the loop of the jejunum requires much less work than closure of the stomach and performance of a gastroenterostomy of the usual posterior type. In our experience, it makes no difference whether the jejunum is brought up anterior or posterior to the colon. The deciding factor should be the length of the mesentery of the jejunum, and the length, vascularity, and thickness of the mesocolon. If the mesocolon is short and thick, or marred with a great many vessels, it would certainly be desirable to bring the jejunum up anteriorly if the mesentery will allow it to reach the end of the common duct without tension. The anterior position is desirable from the standpoint of consumption of time, since it will naturally take several minutes to anchor the edge of the opening in the mesocolon to the two loops of jejunum after they are brought up posterior to the colon.

As yet there is no agreement as to whether or not the stump of the pancreas should be closed tightly or be transplanted into the stomach or jejunum. Brunschwig[8] and others have expressed the opinion that so little ill effect is sustained by closure of the pancreas that indications for transplantation are insufficient to warrant the time required. The amount of unabsorbed fat in the feces after operation, as reported by various authors (Whipple,[1] Dennis,[10] Brunschwig and Allen[12]), varies tremendously. The latter authors report the wide variation of 91.2, 96, and 8.4 per cent in three cases studied; in the first of these cases the unabsorbed fat dropped from 91.2 to 65 per cent under pancreatin therapy. It is true that practically all of these pancreatic fistulas will close spontaneously after several weeks, and that rarely are any nutritional disturbances encountered. However, we do have one patient who has had a fistula for seven months and who developed a diarrhea with profound weakness for several weeks after operation. He improved under strict dietetic care and pancreatin, but still has a pancreatic fistula and is not gaining weight. One other important point in a discussion about transplantation of the stump of the pancreas into the intestine is a question as to whether or not the pancreatic duct will remain open. At the present time we have no information to answer this question. It would naturally not be desirable to take the time to transplant the stump of the pancreas if the duct were going to close within a short time after transplantation. However, we do know that the duct remains open for several weeks. Transplantation might, therefore, improve the immediate convalescence. We predict that as time goes on there will be a tendency to transplant the stump of the pancreas, at least on some occasions. Poth[13] recommends transplantation of the pancreatic duct into the jejunum and reports the use of a small silver tube to maintain patency of the duct.

We are convinced of the desirability of hooking up the jejunum in such a way that the food stream will not flow over the site of transplantation of the common duct into the jejunum. We believe that infection of the cholangitis type will be minimized if the food stream does not flow over the transplanted common duct. It is true that suppurative cholangitis in these operations is not very common, but it is being observed by many surgeons performing the operation. For example, Whipple[1] stated that he had abandoned the cholecystojejunostomy because of a possible "blowout" of the common duct or infection with development of cholangitis. Child[9] stated that "although the gall bladder was utilized in Cases 2, 3, 4, and 5 without the development of any immediate postoperative complications, troublesome attacks of acute cholangitis marred the

result in Case 4." In a resection of the stomach and head of the pancreas, performed by one of us, not herein reported because the tumor was primary in the stomach, death was caused primarily by a suppurative cholangitis; the common duct had been tied and the gall bladder anastomosed to the jejunum. If suppurative cholangitis occurs in no more than 5 or 10 per cent of cases it would appear worth while to attempt to modify the procedure in such a way as to avoid this complication. As a matter of fact, we have encountered suppurative cholangitis in several of our patients upon whom we performed a plastic operation upon the common duct for benign stricture, but true enough it usually occurred in those cases in which a vitallium tube was used at the anastomotic line between the common duct and jejunum; on two occasions we were able to prove that the food or secretions entering the biliary system were the cause of the cholangitis because the chills and fever stopped abruptly when we interrupted the loop of jejunum which had allowed reflux of food into the intrahepatic ducts through the vitallium tube.* Although there is no concrete evidence that hooking up the loop of intestine with the common duct distal to the gastric stoma would result in less cholangitis than when it is hooked up proximal to the gastric stoma, it appears worth while to resort to the latter plan since the amount of operative work is the same. Perhaps a more prominent reason for rotating the jejunum so that the food stream will pass downward as in Fig. 1*F*, rather than upward as in Fig. 1*A*, is the fact that in the former instance the food can empty from the stomach into the intestine by *gravity* and will not have to be forced *upward* to make the turn into the jejunum.

ABSTRACT OF CASE REPORTS

CASE 1.—Patient G. S., a Negro woman, aged 49 years, entered the Illinois Research Hospital, April 3, 1944, complaining of jaundice. The onset was three years before, with development of painless jaundice accompanied by severe itching. Stools were clay-colored. After three months, symptoms cleared and she was relatively asymptomatic. A second attack developed one year before admission and, like the first, consisted of onset of painless jaundice with itching. In August, 1943, laparotomy was performed elsewhere, and a large distended gall bladder removed. Bile drained from the wound for two months. After the biliary fistula closed, jaundice and itching again developed.

Physical Examination.—The patient was intensely jaundiced; there were numerous scratch marks on the skin. No masses were felt in the abdomen except for the liver edge which was felt about two fingerbreadths below the costal margin. The rest of the examination was relatively negative.

Laboratory Examination.—Red blood cells, 2.8 million; hemoglobin, 6.5 Gm.; white blood cells, 11,700. Urine was negative except for large quantities of bile. The serum albumin was 3.0 and serum globulin 2.5 Gm. per cent. Blood chlorides and nonprotein nitrogen were normal. Icterus index was 53; blood amylase 326 (normal 80 to 150). Stool was acholic.

After numerous transfusions, laparotomy was performed, May 1, 1944. Numerous adhesions were present; a small stump of the gall bladder remained. In the duodenum at the site of the ampulla of Vater was an irregular, indurated mass about 3 by 5 cm. This appeared definitely to be carcinoma, and presumably was arising from the head of the pancreas or ampulla of Vater, probably the latter. No metastases were present. We, therefore, decided upon a resection. The duodenum and head of the pancreas were removed according to the technique previously described in this report. The distal end of the duodenum was turned in with a double row of catgut sutures, the upper end being cut at the pylorus. The loop of jejunum was brought up anterior to the colon for anastomosis with the common duct and stomach. The cut end of the pancreas was closed with interrupted cotton sutures. An end-to-side anastomosis was done between the end of the stomach and the jejunum (see

*These patients will be discussed in detail in another publication dealing with plastic operations on the common duct, utilizing vitallium tubes.

Fig. 2). The common duct was transplanted into the jejunum proximal to the gastric anastomosis so that food would not flow over the opening of the transplanted common duct.

Microscopic diagnosis was papillary adeno- and gelatinous carcinoma of the ampulla of Vater involving the duodenal wall and head of the pancreas. Convalescence was unusually smooth and the patient left the hospital on the sixteenth postoperative day. When last seen, six months after operation, she had recovered except that she still felt a bit weak and was still twenty-five pounds under her pre-illness weight. The pancreatic fistula drained for four months but caused very little irritation of the skin.

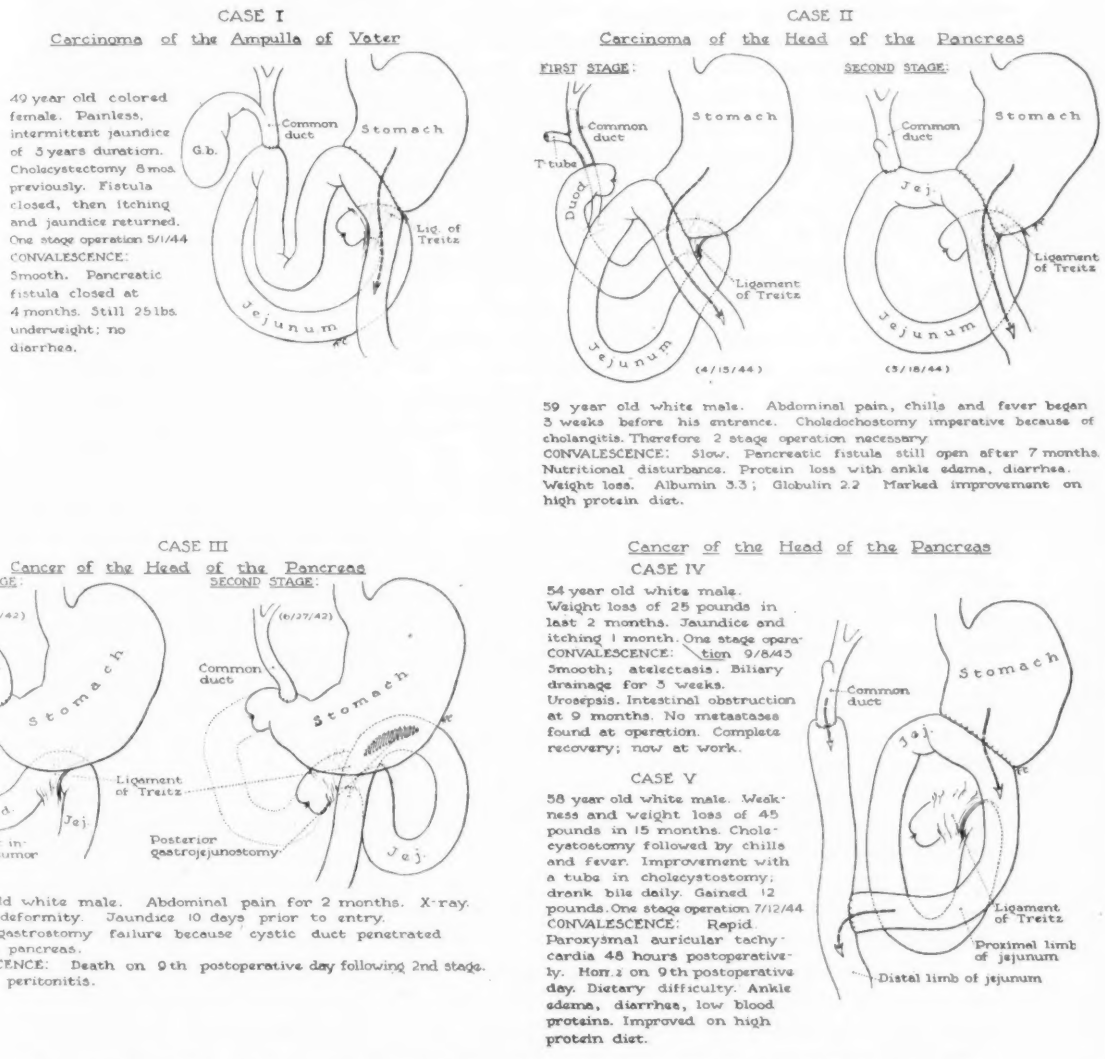
CASE I
Carcinoma of the Ampulla of Vater
49 year old colored female. Painless, intermittent jaundice of 3 years duration. Cholecystectomy 8 mos. previously. Fistula closed, then itching and jaundice returned. One stage operation 5/1/44
CONVALESCENCE: Smooth. Pancreatic fistula closed at 4 months. Still 25 lbs. underweight; no diarrhea.
G.b.
Common duct
Stomach
Lig. of Treitz
Jejunum
CASE II
Carcinoma of the Head of the Pancreas
FIRST STAGE:
Common duct
Stomach
T tube
Duod.
Ligament of Treitz
Jejunum
(4/15/44)
SECOND STAGE:
Common duct
Stomach
Jej.
Ligament of Treitz
Jejunum
(5/18/44)
59 year old white male. Abdominal pain, chills and fever began 3 weeks before his entrance. Choledochostomy imperative because of cholangitis. Therefore 2 stage operation necessary
CONVALESCENCE: Slow. Pancreatic fistula still open after 7 months. Nutritional disturbance. Protein loss with ankle edema, diarrhea. Weight loss. Albumin 3.3; Globulin 2.2 Marked improvement on high protein diet.
CASE III
Cancer of the Head of the Pancreas
FIRST STAGE:
(6/15/42)
G. b.
Stomach
Duod.
Jej.
Cystic duct involved in tumor mass.
SECOND STAGE:
(6/27/42)
Common duct
Stomach
Ligament of Treitz
Posterior gastrojejunostomy
Jej.
60 year old white male. Abdominal pain for 2 months. X-ray: Stomach deformity. Jaundice 10 days prior to entry. Cholecystogastrostomy failure because cystic duct penetrated tumor in pancreas.
CONVALESCENCE: Death on 9th postoperative day following 2nd stage.
Autopsy: peritonitis.
Cancer of the Head of the Pancreas
CASE IV
54 year old white male. Weight loss of 25 pounds in last 2 months. Jaundice and itching 1 month. One stage operation 9/8/43
CONVALESCENCE: Smooth; atelectasis. Biliary drainage for 3 weeks. Urosepsis. Intestinal obstruction at 9 months. No metastases found at operation. Complete recovery; now at work.
CASE V
58 year old white male. Weakness and weight loss of 45 pounds in 15 months. Cholecystostomy followed by chills and fever. Improvement with a tube in cholecystostomy; drank bile daily. Gained 12 pounds. One stage operation 7/12/44
CONVALESCENCE: Rapid. Paroxysmal auricular tachycardia 48 hours postoperatively. Hem. on 9th postoperative day. Dietary difficulty. Ankle edema, diarrhea, low blood proteins. Improved on high protein diet.
Stomach
Common duct
Jej.
Ligament of Treitz
Proximal limb of jejunum
Distal limb of jejunum

Fig. 3.—Summary of our own five cases of pancreaticoduodenectomy, illustrating the types of operation in each patient. The method illustrated in Case 1 is the one preferred by us.

CASE 2.—Patient E. K. was a white man, 59 years old, who entered the Illinois Research Hospital, April 6, 1944, complaining of pain in the abdomen, chills, fever, and jaundice of three weeks' duration. Pain was greatest just to the left of the umbilicus and radiated throughout the abdomen. There was a history of epilepsy of several years' duration.

Physical Examination.—The patient was emaciated and deeply jaundiced. The temperature was 102° F. The abdomen was quite tender to palpation throughout, particularly in the right upper quadrant where the liver was felt to be enlarged about 6 cm. beyond the costal margin.

Laboratory Examination.—Red blood cells, 4.7 million; white blood cells, 9,500; blood chlorides, nonprotein nitrogen, and blood proteins were normal. The icterus index was 82.

The patient continued to have a septic type of fever indicating that a suppurative cholangitis was present. Accordingly, April 15, 1944, a *laparotomy* was performed. A

choledochostomy was done and purulent material was obtained from the common duct. The head of the pancreas was enlarged and very hard; the diagnosis of carcinoma seemed obvious. No metastases were present and the tumor appeared operable. The patient was obviously too ill for a one-stage operation to be considered. However, an end-to-side posterior gastrojejunostomy was performed in addition to the choledochostomy. The cut end of the duodenum was closed with two layers of sutures. The patient recovered slowly, although the fever subsided rapidly following drainage of the common duct.

May 18, 1944, the *second operation* was performed. The head of the pancreas and duodenum were resected, turning in the distal duodenum. The cut end of the pancreas was closed with interrupted cotton sutures. The common duct was transplanted into the jejunum proximal to the gastrojejunostomy. He was discharged four weeks after the second operation but a few weeks later developed a diarrhea which resulted in extreme weakness and an additional weight loss of three or four pounds. In addition, he developed considerable ankle edema. The serum albumin was 3.3 and serum globulin 2.2 Gm. per cent. There was likewise still profuse drainage from the pancreatic fistula. He was readmitted on the medical service and given choline, pancreatin, and a high protein diet. The diarrhea and edema of the extremities disappeared within one week. At the present time, seven months after his second operation, the pancreatic fistula is still draining several hundred cubic centimeters per day. A third laparotomy is contemplated to transplant the stump of the pancreas into the jejunum.

CASE 3.—Patient R. S. J. (Hospital No. 21738), a white man, aged 69 years, entered St. Luke's Hospital, June 1, 1942, complaining of severe constant epigastric pain for the previous two months. Pain was constant (not colicky), and unrelated to food intake. It interfered with his sleep and did not radiate. He had lost thirty pounds during the last two months. Urine had been dark and stools white only during the past week. Icterus was present only for two days preceding admission. The physician who originally saw the patient noticed a filling defect in the stomach which he thought to be carcinoma. The patient postponed surgery because he was working and felt he needed the money.

Physical Examination.—Temperature, pulse, and respirations were normal. Blood pressure was 150/64. No masses were felt in the abdomen, although an indefinite sense of resistance was noted in the right upper quadrant. A diagnosis of carcinoma of the head of the pancreas or carcinoma of the stomach with metastases was made.

Laboratory Examination.—The Kahn test was negative. Urine was normal except for bile. Icterus index was 15; serum protein 7.06 grams per cent; blood chlorides 640; nonprotein nitrogen, 40; red blood cells, 5.1 million. No bile was found in the stool but the benzidine test was slightly positive.

June 13, 1942, *laparotomy* was performed. A carcinomatous mass was found in the head of the pancreas and considered operable. *Cholecystogastrostomy* was done as a first stage operation.

June 22, icterus index was 40. June 29, glucose tolerance test was normal. Stool showed a large amount of fat. June 30, there was no benefit shown from cholecystogastrostomy; jaundice was deepening.

June 27, 1942, the *second operation* was done. Pancreaticoduodenectomy and posterior side-to-side gastrojejunostomy were performed. The gall bladder was removed because the cystic duct was blocked by the tumor of the pancreas. (This explained the lack of benefit from cholecystogastrostomy.) The common duct was implanted into the stomach. Obstructive biliary cirrhosis of the liver was also present.

July 2, 1942, red blood cells, 4.6 million; hemoglobin, 13. July 3, amylase, 0; blood chlorides, 615; carbon dioxide, 61.4 volumes per cent. The patient did well until July 6, when a sudden turn for the worse occurred. He died on July 9; clinically "hepatic insufficiency" appeared to be an important factor in his downward progress.

Autopsy revealed generalized acute serofibrinous peritonitis; a localized abscess and hemorrhage were noted in the fibrinous adhesions in the region of the ligamentum hepatoduodenale. The impression at the time was that the peritonitis was not in itself enough to be fatal. The sutures in the superior mesenteric vein had produced no thrombus.

Microscopic examination of the specimen removed July 1, 1942, revealed a primary carcinoma of the head of the pancreas.

CASE 4.—Patient J. B. (Hospital No. 43-37636), a white man, entered Cook County Hospital, Aug. 13, 1943. Aside from large veins and swelling of the legs, the history was

negative until about two months before, when he began to note that he had been losing some weight. One month before admission jaundice began to appear. In the previous two months he had lost twenty-five pounds. Itching had been associated with jaundice.

Physical Examination.—The temperature was 98.6° F.; pulse, 80; respirations, 22; blood pressure, 106/58. The skin was lemon yellow in color. Slight nasal deformity was present. The chest was kyphotic and emphysematous. The liver margin was down at least 7 cm. Bilateral pitting edema of the lower extremities was present. Rectal examination revealed clay-colored feces. A diagnosis of carcinoma of the pancreas was made.

Laboratory Examination.—Bile was present in the urine to a 4 plus degree, but no albumin. Blood: red blood cells, 3.8 million; hemoglobin, 70. X-ray: no apparent pathologic findings were noted in the stomach or duodenum. Aug. 16, 1943, nonprotein nitrogen, 35; creatinine, 1.7; serum albumin, 3.6; serum globulin, 2.4; Takata-Ara, 1 plus.

Aug. 27, 1943, blood cholesterol, 552; esters, 222. Sept. 3, blood amylase, 16 (normal 80 to 150). Sept. 4, nonprotein nitrogen, 27; serum albumin, 3.4; serum globulin, 2.5; red blood cells, 4.3 million; hemoglobin, 80.

Laparotomy.—Sept. 8, 1943, one-stage resection of the head of the pancreas was performed. The tumor was small. A few lymph nodes were present but they did not appear to be carcinomatous. (Biopsy of the pancreas at that time was positive for carcinoma.) A resection of the stomach (posterior polya technique), duodenum, and pancreas was performed along with a cholecystectomy. The common duct was anastomosed to the jejunum utilizing the Roux principle.

Sept. 9, 1943, the patient developed massive atelectasis which was relieved by hyperventilation and cough. Sept. 25, icterus index, 37. Considerable biliary drainage noted. Oct. 3, chill; urinary tract infection. Oct. 5, cystoscopy. The patient had severe generalized cystitis with a contracture of the vesical neck and three ounces of residual urine. There was no upper urinary tract instrumentation.

Oct. 20, bile drainage had ceased. Stools showed bile and a moderate amount of undigested fat. The odor was very foul. Nonprotein nitrogen, 23; serum albumin, 3.4; serum globulin, 1.7. Oct. 22, the patient was discharged. At no time did he have a pancreatic fistula.

Nov. 23, 1944, patient has been seen repeatedly since. He had a small suprahepatic abscess drained about nine months after the original operation. At that time no metastases were seen. He is now working and is apparently well.

CASE 5.—Patient C. S. (Hospital No. 55167), a white man, aged 58 years, was admitted to St. Luke's Hospital, July 1, 1944. His health was good until fifteen months before, at which time he noted progressive weakness with no apparent cause. He was treated until January, 1944, without relief. He had lost forty-five pounds in the nine-month interval.

In February he had a gall bladder visualization at another hospital and a pathologic gall bladder was found; February 24, the gall bladder was drained and a single gallstone removed. Since that time he has had a draining incision; especially profuse after meals. (Jaundice and itching appeared in January.) After the gall bladder drainage, the jaundice and itching disappeared. He has had occasional chills and fever since.

Physical Examination.—The patient was a poorly nourished white man with a slight yellow tint to the skin. The abdomen revealed a sinus from which bile oozed. The blood pressure was 118/74. He had a chill on the day of entrance. Shortly thereafter a catheter was introduced into the gall bladder sinus and better drainage established. No more chills occurred.

Laboratory Examination.—Red blood cells, 5.3 million; hemoglobin, 15.1 Gm.; white blood cells, 9.9; Kahn, negative; nonprotein nitrogen, 25.2; blood chlorides, 575 phosphorus, 3.67; vitamin C, 0.6; phosphatase, 9.63; icterus index, 15; prothrombin time, 35 seconds; serum albumin, 3.5; serum globulin, 2.02; hematocrit, 43; urine, negative.

The patient was given a high protein diet with vitamin K and he drank bile daily. He gained ten pounds in the twelve days between entrance and operation.

Operation.—July 12, 1944, one-stage resection of the duodenum and head of the pancreas was performed. A Polya anastomosis and choledochojejunostomy of the Roux type were performed, both retrocolic. The patient was given 2,000 c.c. of blood while on the operating table. Three holes were accidentally made in the superior mesenteric vein, which required considerable time for repair.

July 14, 1944, the postoperative course was uneventful except for development of auricular flutter (?). The pulse rose to 180 but responded well to six doses of quinidine (gr. 3).

July 21, the patient left the hospital, nine days after the operation.

ANALYSIS OF CASES

Of the five cases herein reported, all the patients had primary carcinoma of the head of the pancreas except one (Case 1), who had a primary carcinoma of the ampulla of Vater with invasion of the duodenum. Two two-stage resections were performed and three one-stage resections. The decision to perform a two-stage operation was mandatory in one patient because of a severe suppurative cholangitis which was present on admission. In two patients a one-stage operation with performance of an end-to-side gastrojejunostomy (posterior Polya technique) with a choledochojejunostomy after the Roux principle as recommended by Whipple[14] in 1938 was performed (see Fig. 1). Although these two patients are alive and doing well fourteen and four months, respectively, since operation, we prefer the technique performed in Case 1 (see Fig. 2) largely because it requires less operative work.

As noted in Fig. 3, a pancreatic fistula developed in two of the five patients. In one of these, seven months after operation the fistula is still draining. The diarrhea and edema of the ankles which developed five to six weeks after operation have disappeared; an operation to transplant the stump of the pancreas into the jejunum is now contemplated. In this patient there has been considerable pain in the region of the fistula, particularly during short intervals when the fistula was closed or draining only a small amount of pancreatic secretion.

Of the five cases herein presented, one patient died; this constitutes a mortality rate of 20 per cent. An insufficient length of time has elapsed since operation to determine the prospects of a five- or ten-year cure.

SUMMARY

A new operation for resection of the duodenum and head of the pancreas for carcinoma is described. In this procedure a long loop end-to-side anastomosis is made between the stomach and the jejunum distal to the choledochojejunostomy. This secures drainage of the biliary tract proximal to the gastric anastomosis and so avoids the danger attendant upon passage of food over the common duct opening. However, the chief advantage of the technique recommended lies in the requirement of less time for performance of the operation; in our estimation suture lines and anastomoses for resection of the duodenum and head of the pancreas are reduced to a minimum. The jejunum is anastomosed to the cut end of the stomach with the distal end to the greater curvature so that the food passes downward by gravity into the jejunum instead of upward into the jejunum as it must in many operations previously recommended.

The chief purpose of the long loop proximal to the end-to-side gastrojejunostomy is to allow transplantation of the common duct and, if desired, the stump of the pancreas, into the jejunum proximal to the gastric anastomosis. Although to date very few surgeons are transplanting the stump of the pancreas into the intestine, we believe this procedure will in the future be performed more often than it is now. In one of our patients, the pancreatic fistula which followed the resection is still draining seven months after operation although now only a few ounces per day.

Four patients with carcinoma of the head of the pancreas and one with carcinoma of the ampulla of Vater have been subjected to radical resection of the duodenum and head of the pancreas. There has been one fatality.*

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*Since submission of this article for publication a sixth resection has been performed, utilizing the preferred procedure as illustrated in Fig. 2; the stump of pancreas was transplanted into the loop of jejunum. Postoperative convalescence was uneventful but since only six weeks have passed, insufficient time has elapsed to determine ultimate results.

PANCREATICODUODENECTOMY FOR CARCINOMA OF THE AMPULLA AND AMPULLARY REGION

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NINE years have passed since Whipple, Parsons, and Mullins[44] reported their cases of successful resection of the head of the pancreas and duodenum for carcinoma of the ampulla. During these nine years many surgeons have interested themselves in the treatment of carcinoma arising in the ampulla and ampullary region, and many modifications of the technique suggested by Whipple and his associates have been described. The fear that existed for many years, that surgical attack upon the pancreas containing a carcinoma was too great, no longer exists as manifested by the number of operations done since 1935. Whipple[48] recorded sixty-four cases of radical pancreaticoduodenectomy which he had collected from published records and from personal reports up to April 1, 1942. Since then thirty-five cases have been found recorded in the surgical literature (Table I). Five cases are added in this report making a total of 104. There are undoubtedly many unrecorded cases, but to avoid confusion in a study of the results of the operation, no effort has been made to collect such cases.

Pancreaticoduodenectomy for carcinoma of the ampulla and ampullary area will be discussed under the following headings:

1. Diagnosis at operation
2. Is radical pancreaticoduodenectomy justifiable?
3. Is restoration of the external pancreatic secretion advisable?
4. Choice of one-stage or two-stage operation
5. Choice of technique of pancreaticoduodenectomy
6. Comments upon personal cases

DIAGNOSIS AT OPERATION

Some difficulty may be experienced in making a diagnosis of carcinoma in the ampullary region when the operative field is exposed. Chronic pancreatitis or a benign adenoma may so closely simulate carcinoma that a diagnosis made by palpation alone may lead to a needlessly serious operation. The importance of this statement is clearly emphasized by the case of benign tumor of the ampulla reported by Horsley[18] and the case of chronic pancreatitis recorded in Table II; both patients were subjected to pancreaticoduodenectomy. It is also true that a diagnosis of carcinoma may be made, considered incurable, and proved to be wrong by many years of subsequent good health as shown by Kiefer and Moravec.[22] A stone impacted at the ampulla may be mistaken for carcinoma. If in doubt, a correct diagnosis of stone can easily be made by duodenotomy.

A thorough exploration of the liver, head of the pancreas, and regional lymph nodes should be made. In selected doubtful cases a duodenotomy and biopsy of the papillary area may be indicated or a biopsy of lymph nodes or pancreas may be advisable. If the diagnosis is not clear after a biopsy of the

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papilla, lymph nodes, or head of the pancreas, it is wise to plan the operation in two stages and complete the second stage after a positive diagnosis of an operable carcinoma is made. If gross or microscopic evidence of carcinoma is found in the regional lymph nodes or liver, the second stage of the operation should be abandoned. It is doubtful if life can be prolonged by a palliative pancreaticoduodenectomy when proved metastases are present.

IS RADICAL PANCREATICODUODENECTOMY JUSTIFIABLE?

In a discussion of a paper by Harvey and Oughterson,[17] in 1942, Whipple[48] stated that radical operation for carcinoma of the ampullary region "is still unquestionably in the experimental stage."

It is generally believed that carcinomas arising in the papilla of vater or ampulla grow slowly and metastasize late. Baggenstoss[1] supported this belief in his report that fifteen of twenty-eight carcinomas of the papilla of vater did not show metastases at necropsy. If this assumption is true, a high percentage should be curable by radical operation. Considering the number of patients who have survived the radical operation and later died of metastases, the belief that the growth of the carcinoma is local for a very long period of time becomes less impressive. Five of the eight patients on whom I did pancreaticoduodenectomy died of metastases. Although the results of the cases reported from April 1, 1942, to Nov. 1, 1944, are incomplete, metastases were present at death, at operation, or were noted before death in six of twenty cases with follow-up records.

There has been no accurate publication of the final results of pancreaticoduodenectomy. Until a careful study is made, it will be difficult to state with any degree of accuracy what percentage of cures may result or what the average length of life will be following this operation. It is also difficult at present to compare and draw conclusions from the results obtained by the palliative operation, the transduodenal resection, and the radical operation (Tables III, IV, and V). The data available are not very convincing that pancreaticoduodenectomy is superior to less radical measures. Regardless of our lack of knowledge of final results, radical excision of a carcinoma arising in the ampullary region by the Whipple type of operation fulfills the requirements of cancer surgery in general and offers the greatest hope for the greatest number of cures in the future.

IS RESTORATION OF THE EXTERNAL PANCREATIC SECRETION DESIRABLE?

In 1908, Sauvé[38] stated that from the physiologic standpoint the head of the pancreas may be resected without anastomosis of the duct of Wirsung to the intestines. Berg and Zucker[3] described fatty degeneration of the liver in experimental animals after ligation of the pancreatic ducts. It is reasonable to expect that fat digestion would be disturbed by excluding the external pancreatic secretion, but Whipple, Parsons, and Mullins,[44] in their first cases of radical pancreaticoduodenectomy, found that 80 to 90 per cent of the fat was absorbed. They suggested that there might be a compensatory secretion of a fat-splitting ferment in the upper intestine. According to Montgomery,[26] experimental ligation of the pancreatic ducts results in atrophy of the pancreatic acinar structures and fatty infiltration of the liver. He warned that obstruction of the secretory mechanism of the pancreas in patients will lead to major disturbances of the individual's ability to control his lipid metabolism, which must be controlled by replacement therapy. Cole and Howe[11] recognized the relationship between disease of the pancreas and fatty infiltration of the liver.

TABLE I. LIST OF COLLECTED CASES FROM APRIL 1, 1942 (DATE OF WHIPPLE'S REPORT) TO NOV. 1, 1944

AUTHOR	DATE REPORTED	AGE	SEX	TYPE OF OPERATION	RESULT
Zinninger[49]	June, 1942	62	M	Two-stage: First stage: End-to-side jejunojejunostomy and cholecystojejunostomy Second stage: Posterior gastroenterostomy, pancreaticoduodenectomy and closure of stump of pancreas; seventeen mo. later pancreatic duct and bowel united with vitallium tube	In good health after 2½ yr.
Orr[28]	June, 1942	65	F	Two-stage: First stage: Cholecystogastrostomy Second stage: Posterior gastroenterostomy, pancreaticoduodenectomy, pancreaticojejunostomy and jejunojejunostomy	Alive 3 mo. after operation
Orr	June, 1942	56	F	One-stage: Posterior gastroenterostomy, pancreaticoduodenectomy; choledochojejunostomy, pancreaticojejunostomy and jejunojejunostomy	Alive 3 mo. after operation
Gordon-Taylor[15]	Aug., 1942	60	M	One-stage: Cholecystogastrostomy, posterior gastroenterostomy, pancreaticoduodenectomy, and closure of stump of pancreas	Death 5 days after operation; anuria
Gordon-Taylor	Aug., 1942	58	M	Two-stage: First stage: Jejunum sectioned, end-to-side jejunojejunostomy and cholecystojejunostomy Second stage: Posterior gastroenterostomy, pancreaticoduodenectomy, and closure of stump of pancreas	Death in 6 mo.; hepatic metastases
Gordon-Taylor	Aug., 1942	60	F	Two-stage: First stage: Cholecystogastrostomy Second stage: Posterior gastroenterostomy, pancreaticoduodenectomy, and closure of stump of pancreas	Alive and well 21 mo. after operation
Dennis[13]	Aug., 1942	64	M	One-stage: Pancreaticoduodenectomy, hemigastrectomy, closure of stump of pancreas, Polya type of gastrojejunostomy, and cholecystojejunostomy	Alive with recurrence after 6½ mo.
Dennis	Aug., 1942	67	M	One-stage: Pancreaticoduodenectomy, hemigastrectomy, closure of stump of pancreas; Polya type of gastrojejunostomy and choledochojejunostomy	Postoperative death; autopsy, metastases not mentioned

Pearse[31]	Sept., 1942	56	F	One-stage: Pancreaticoduodenectomy, cholecystojejunostomy, end-to-side gastrojejunostomy, and closure of stump of pancreas	Left hospital on 58th postoperative day; no later report (proved to be primary carcinoma of duodenum)
Lake, Cornell, and Harrison[24]	Jan., 1943	25	F	Two-stage: First stage: Cholecystojejunostomy, section of jejunum, and end-to-side jejunojejunostomy; biopsy Second stage: Posterior gastroenterostomy, partial gastrectomy, and pancreaticoduodenectomy	Alive 1 yr. after operation; recurrence probable, metastases found in lymph nodes at operation
Phillips[33]	April, 1943	44	M	Two-stage: First stage: Exploration of common duct, duodenotomy, cauterization and biopsy of tumor, choledochogastrostomy, anterior gastroenterostomy, and jejunojejunostomy. Second stage: Pancreaticoduodenectomy, ligation of pancreatic duct, and closure of stump of pancreas	Recovered from operation; no later report
Sternfeld and Meffley[39]	May, 1943	56	M	Two-stage: First stage: Cholecystoduodenostomy Second stage: Detached cholecystoduodenostomy, pancreaticoduodenectomy, closure of stump of pancreas, anterior gastroenterostomy, and cholecystojejunostomy	Died four weeks after second stage of operation
Cattell[8]	June, 1943	?	?		Survived operation
Cattell	June, 1943	?	?	One-stage: Pancreaticoduodenectomy including pyloric end of stomach, four divisions of duodenum and small proximal portion of jejunum, end-to-end gastrojejunostomy, end-to-side pancreaticojejunostomy, end-to-side choledochojejunostomy over a tube, and jejunojejunostomy	Survived operation
Cattell	June, 1943	?	?		Survived operation
Cattell	June, 1943	?	?	Two-stage: First stage: Antecolic cholecystojejunostomy Second stage: Pancreaticoduodenectomy, antecolic gastrojejunostomy, pancreaticojejunostomy, and jejunojejunostomy	Survived operation
Cattell	June, 1943	?	?	Type and details of operation not recorded	Death on 17th postoperative day

TABLE I.—CONT'D

AUTHOR	DATE REPORTED	AGE	SEX	TYPE OF OPERATION	RESULT
Rekers, Pack, and Rhoads[36]	Aug., 1943	39	F	Two-stage: First stage: Cholecystogastrostomy Second stage: Posterior gastroenterostomy, pancreaticoduodenectomy, closure of stump of pancreas	Alive 1 yr. after operation
Dragstedt, Julian, Allen, and Owens[14]	Aug., 1943	67	M	One-stage: Cholecystectomy, pancreaticoduodenectomy, closure of stump of pancreas, end-to-end gastroduodenostomy, and hepaticogastrostomy	Died 4 mo. after operation
Gray and Sharpe[16]	Dec., 1943	58	?	Two-stage: Modified Whipple technique; no details of operation	Died of peritonitis 8 days after second stage
Brunschwig[5]	Dec., 1943	58	?		Death on 4th postoperative day
Brunschwig	Dec., 1943	71	?		Death on 3rd postoperative day
Brunschwig	Dec., 1943	57	?		Died 5 mo. and 3 weeks after operation
Brunschwig	Dec., 1943	46	?	One-stage:	Alive 6 mo. after operation
Brunschwig	Dec., 1943	54	?	Pancreaticoduodenectomy with resection of stomach through antrum and 3 to 6 cm. of jejunum, posterior gastrojejunostomy, choledochojejunostomy, jejunojejunostomy, and closure of stump of pancreas	Death on 8th postoperative day; metastases found at operation
Brunschwig	Dec., 1943	35	?		Died 5 mo. after operation; metastases
Brunschwig	Dec., 1943	73	?		Died on 8th postoperative day
Brunschwig	Dec., 1943	55	?		Alive 6 mo. after operation
Watson[41]	Apr., 1944	43	F	Two-stage: First stage: Antecolic cholecystojejunostomy Second stage: Pancreaticoduodenectomy, section of jejunum and end-to-end gastrojejunostomy, and end-to-side jejunojejunostomy	Alive 182 days after operation

Poth[35]	May, 1944	72	M	One-stage: Pancreaticoduodenectomy with partial resection of stomach and 18 in. of jejunum, fundus-to-end cholecystojejunostomy, pancreaticojejunostomy (silver cannula in duct), end-to-side gastrojejunostomy	Alive 4 mo. after operation
Child[9]	June, 1944	56	F	Two-stage: First stage: Duodenostomy and biopsy, posterior gastrojejunostomy, cholecystogastrostomy, and ligation of common duct Second stage: Pancreaticoduodenectomy, closure of stump of pancreas, and later jejunostomy for feeding	Died 45 days after second operation
Child	June, 1944	52	M	Two-stage: First stage: Cholecystogastrostomy and posterior gastrojejunostomy Second stage: Pancreaticoduodenectomy and closure of stump of pancreas	Died 8 mo. after operation
Child	June, 1944	57	M	One-stage: Pancreaticoduodenectomy, end-to-end retrocolic pancreaticojejunostomy, antecolic gastrojejunostomy, and antecolic side-to-side cholecystojejunostomy	Exploration of abdomen 15 mo. and 20 days after operation revealed general carcinomatosis (proved to be primary carcinoma of duodenum)
Child	June, 1944	69	M	One-stage: Pancreaticoduodenectomy, cholecystojejunostomy, retrocolic end-to-end pancreaticojejunostomy, retrocolic end-to-side gastrojejunostomy	Alive and well 1 yr. after operation
Child	June, 1944	55	F	One-stage: (Previous local excision of tumor of ampulla through duodenum) Pancreaticoduodenectomy, retrocolic end-to-end pancreaticojejunostomy, retrocolic end-to-side choledochojejunostomy, retrocolic end-to-side gastrojejunostomy and cholecystostomy	Discharged on 21st postoperative day

TABLE II. PANCREATICODUODENECTOMIES IN THE UNIVERSITY OF KANSAS HOSPITALS FROM APRIL 1, 1940, TO NOV. 1, 1944

PATIENT	SEX	AGE	TREATMENT	RESULT
C. T.*	M	47	Two-stage operation: First stage: Choledochogastrostomy and posterior gastroenterostomy Second stage: Pancreaticoduodenectomy and closure of stump of pancreas	Lived 33 mo.; autopsy, metastases
M. B.†	F	67	Two-stage operation: First stage: Cholecystogastrostomy and posterior gastroenterostomy Second stage: Pancreaticoduodenectomy and closure of stump of pancreas	Lived 22½ mo.; metastases, no autopsy
G. P.‡	F	65	Two-stage operation: First stage: Cholecystogastrostomy Second stage: Posterior gastroenterostomy, pancreaticoduodenectomy, section of jejunum and end-to-side jejunojejunostomy, and pancreaticojejunostomy	Lived 15½ mo.; cause of death unknown, no autopsy
A. B.‡	M	59	One-stage operation: Posterior gastroenterostomy, pancreaticoduodenectomy, choledochojejunostomy, pancreaticojejunostomy, and jejunojejunostomy	Lived 33½ mo.; metastases, no autopsy
B. R.§	M	66	One-stage operation: Cholecystogastrostomy, posterior gastroenterostomy, pancreaticoduodenectomy, and pancreaticoduodenostomy	Primary carcinoma of duodenum; lived 17½ mo.; metastases, no autopsy
M. R.	F	61	Two-stage operation: First stage: Cholecystogastrostomy Second stage: Posterior gastroenterostomy, pancreaticoduodenectomy, and pancreaticoduodenostomy	Lived 21 days; autopsy, chronic pancreatitis
A. M.	F	72	Two-stage operation: First stage: Choledochogastrostomy, duodenotomy, and biopsy of papilla Second stage: Posterior gastroenterostomy, pancreaticoduodenectomy, and pancreaticoduodenostomy	Alive 22 mo. Nov. 1, 1944
M. S.	F	56	One-stage operation: Posterior gastroenterostomy, pancreaticoduodenectomy; section of jejunum and end-to-side jejunojejunostomy, cholecystojejunostomy, and pancreaticojejunostomy	Lived 8½ mo.; metastases, no autopsy
I. F.	M	54	One-stage operation: Pancreaticoduodenectomy, end-to-side gastrojejunostomy, pancreaticojejunostomy, choledochojejunostomy, and jejunojejunostomy	Alive 8 mo. Nov. 1, 1944

*Reported in Surg., Gynec. & Obst. 73: 240, 1941; (included in Whipple's review)[30]
†Reported in Ann. Surg. 114: 602, 1941;[29] (probably included in Whipple's review to April 1, 1942).
‡Reported in Ann. Surg. 115: 1087, 1942[28]
§Reported in Surg., Gynec. & Obst. (in press.)

TABLE III. RESULTS OF PALLIATIVE BILIARY ENTEROANASTOMOSIS

AUTHORS	NUMBER OF CASES FOLLOWED	AVERAGE LENGTH OF LIFE AFTER OPERATION (MO.)	NUMBER OF PATIENTS OPERATED UPON	OPERATIVE MORTALITY (PER CENT)
Judd and Parker,[21] 1928	12	7.7	34	47.0
Coller and Winfield,[12] 1934	19	7.2	30	26.6
Judd and Hoerner,[20] 1935	94	10.2		
Lahey and MacKinnon,[23] 1938	15	8.6		
Zollinger and Kevorkian,[50] 1939	17	9.0	33	21.2
Sallick and Garlock,[37] 1942	25	6.3	50	48.0
Gray and Sharpe,[16] 1943	4	15.5	11	63.6

This relationship they called the "pancreaticohepatic syndrome." Beazell, Schmidt, and Ivy[2] believed that it has been clearly demonstrated that exclusion of pancreatic juice from the intestine results in a decided increase in the quantity of fat, nitrogen, starch, and the total carbohydrate eliminated in the feces. In a study of achylia pancreatica, as a result of chronic pancreatitis, these investigators found that the oral administration of pancreatic enzymes (Pancreatin) is of value in reducing the excess of both fat and nitrogen in the feces. The conclusions of Ivy and his co-workers were not substantiated by Whipple and Bauman,[47] who reported that normal fat absorption is possible when no pancreatic juice enters the intestine. Metabolic studies of a patient with a pancreaticoduodenectomy for carcinoma with exclusion of the external pancreatic secretion made by Lake, Cornell, and Harrison[24] have shown that pancreatic enzyme therapy (Holadin) markedly reduced the loss of protein and fat in the feces but did not materially affect the loss of calcium. Studies similar to those of Lake and his associates were made by Rekers, Pack, and Rhoads.[36] These authors concluded that the administration of pancreatin resulted in definite clinical improvement of the patient and definitely decreased the quantity of fat and nitrogen in the feces. They also found that administration of lipocaic was without significant effect. Three patients with pancreaticoduodenectomies were studied by Brunschwig and Allen.[4] In two of their patients bulky fatty stools developed with a radical reduction in fat absorption. In the third patient fat absorption was normal. They remark that the basis for the variation in fat absorption following exclusion of the pancreatic juice in man remains obscure. The two patients having disturbed absorption came to autopsy five and five and one-half months after operation. In each case the pancreas showed marked fibrosis and atrophy of the acinar tissue. Brunschwig[7] ligated the pancreatic duct of a monkey and the animal lived four years with no evidence of significant physiologic disturbance during this period. At autopsy the immediate cause of death of the monkey was not apparent. There was complete absence of the pancreatic acinar tissue.

Some doubt has been expressed by Brunschwig as to whether appreciable pancreatic secretion exists after implantation of the pancreatic stump into the

TABLE IV. RESULTS OF LOCAL EXCISION OF TUMOR; TRANSDUODENAL EXCISION, EXCISION OF TUMOR WITH SECTION OF DUODENUM, AND RETRODUODENAL EXCISION

AUTHORS	NUMBER OF CASES FOLLOWED	AVERAGE LENGTH OF LIFE OF PATIENTS DEAD WHEN REPORTED (MO.)	AVERAGE LENGTH OF LIFE OF PATIENTS LIVING WHEN REPORTED	NUMBER OF PATIENTS OPERATED UPON	OPERATIVE MORTALITY (PER CENT)
Hunt[19]	56*	17.4 (24 cases)	32.5 mo. (32 cases)	109	31.1
Gray and Sharpe[16]	5	22.8	0	8	37.5

*Cases of recovery from operation with indicated length of life not included.

TABLE V. RESULTS OF RADICAL PANCREATICODUODENECTOMY

AUTHORS	NUMBER OF CASES FOLLOWED	AVERAGE LENGTH OF LIFE OF PATIENTS DEAD WHEN REPORTED (MO.)	AVERAGE LENGTH OF LIFE OF PATIENTS LIVING WHEN REPORTED (MO.)	NUMBER OF PATIENTS OPERATED UPON	OPERATIVE MORTALITY (PER CENT)
Whipple[46] collected cases to April 15, 1941	28	7.7 (11 cases)	9.3 (17 cases)	41	26.8
Orr collected cases from April 1, 1942, to Nov. 1, 1944 (Table I)	20	5.0 (6 cases)	9.9 (14 cases)	35	25.7
Orr reported personal cases April 1, 1940, to Nov. 1, 1944 (Table II)	9	21.7 (6 cases)*	15 (2 cases)	9	11.1

*Four of these cases are included in the collected cases but reported before death of the patient: One case was a primary carcinoma of the duodenum which has been reported elsewhere (Table II).

alimentary tract. The experimental work of Person and Glenn[32] clearly indicated that the stump of a severed pancreas can be implanted into the alimentary tract without loss of the external pancreatic secretion, atrophy of the pancreas, or fatty infiltration of the liver. After implanting the stump of the pancreas into the stomach, Person and Glenn proved by chemical analysis that the pancreatic secretion was maintained. In one of Child's[9] patients pancreatic enzymes were demonstrated in the intestinal tract following pancreaticojejunostomy and in four of such cases there was no evidence of digestive disturbances following operation. Child also stated that in these four cases there was no instance of pancreatic fistula which has been such a troublesome complication when the stump of the pancreas is closed. Dragstedt[14] noted in animals that a much better nutritive state exists when a remnant of the pancreas with its duct is left connected with the duodenum and suggesed implantation of the pancreatic duct into the stomach or intestine, whenever possible, in man following pancreaticoduodenectomy. In 1943, Whipple[43] recommended the implantation of the stump of the pancreas into the jejunum to improve the existing impaired fat digestion and to avoid the very annoying pancreatic fistula which frequently follows exclusion of the pancreatic secretion. In my own experience pancreatic fistula has not occurred when the stump of the severed pancreas has been anastomosed to the intestine.

Is there any good reason why the end of the divided pancreas should not be united with the intestinal tract? Will future autopsies prove that ascending infections in the pancreas, as a result of pancreaticoenterostomies, shorten the life of patients? Will the proved fibrosis and atrophy of the pancreas following the occlusion of the pancreatic ducts shorten life? Until these questions can be answered, an unqualified opinion concerning the advisability of restoration of the external pancreatic secretion following pancreaticoduodenectomy cannot be given. One can state with assurance that to restore the external pancreatic secretion of the intestinal tract is a physiologic procedure.

CHOICE OF ONE-STAGE OR TWO-STAGE OPERATION

The one-stage operation is preferable if the general condition of the patient will tolerate with reasonable safety such an extensive and prolonged procedure. The earlier patients with periampullary carcinoma come to operation

TABLE VI. MORTALITY RATE OF PANCREATICODUODENECTOMY

		NO. CASES	POST-OPERATIVE DEATHS	POSTOPERATIVE MORTALITY RATE (PER CENT)
Whipple's collected cases to April 1, 1942	Two-stage	41	12	29.2
	One-stage	23	8	34.7
Collected cases April 1, 1942, to Nov. 1, 1944	Two-stage	15	4	26.6
	One-stage	19	6	31.5
Author's added cases*	Two-stage	1	0	0.0
	One-stage	4	1	25.0
Totals	Two-stage	57	16	28.0
	One-stage	46	15	32.6

*Four earlier cases are included in these collected cases.

after the onset of symptoms, the greater the number that will be suitable for the one-stage operation. There will be a relatively large percentage of deeply jaundiced and generally debilitated patients for whom the two-stage operation must be chosen. The first stage of the planned two-stage operation has a sufficiently high mortality to warn the surgeon that the choice of operation must be very carefully made. Statistics to date indicate that the two-stage operation has a slightly lower mortality rate than the one-stage operation (Table VI).

CHOICE OF TECHNIQUE OF PANCREATICODUODENECTOMY

The large number of operative procedures that have been described is obvious evidence that no standard technique has yet been adopted. Almost every surgeon, who has reported his cases, has made some change in the technique (Figs. 1, 2, and 3).

TABLE VII. ADDITIONAL CASES OF CARCINOMA OF AMPULLARY REGION IN HOSPITAL FROM APRIL 1, 1940, TO NOV. 1, 1944

PATIENT	SEX	AGE	TREATMENT	RESULT
J. W.	M	70	Two-stage operation planned: First stage: Cholecystojejunostomy and jejunojejunostomy	Death after first stage on 11th day; autopsy, metastases in liver
H. C.	M	46	Two-stage operation: First stage: Choledochoduodenostomy Second stage: Died on operating table	Died during second stage; autopsy, metastases in lymph nodes
F. K.	M	71	Two-stage operation planned: First stage: Section of jejunum and end-to-side jejunostomy and cholecystojejunostomy	Death after first stage on 10th day; autopsy, metastases to liver
C. B.	F	82	Palliative cholecystogastrostomy	Lived 66 days; metastases found at operation
C. L.	M	64	Palliative cholecystogastrostomy	Hospitalized 21 days; metastases found at operation; lived 5 mo.
T. B.	F	71	Clinical diagnosis of carcinoma of head of pancreas	Died on second hospital day; no autopsy
B. S.	M	68	Clinical diagnosis of carcinoma of head of pancreas	Died on fourth hospital day; no autopsy
C. H.	F	69	Clinical diagnosis of carcinoma of head of pancreas	Discharged on fourth hospital day
A. D.	M	53	Autopsy diagnosis of carcinoma of head of pancreas	Died of advanced pulmonary tuberculosis; autopsy, metastases in liver

A few fundamental principles may be recorded which have a bearing upon the choice of operation. They are (1) removal of sufficient tissue about the tumor to include any local infiltration of the tumor and the regional lymph nodes, (2) use of the common duct for anastomosis, when possible, instead of the gall bladder to facilitate drainage of bile and prevent leakage of bile from

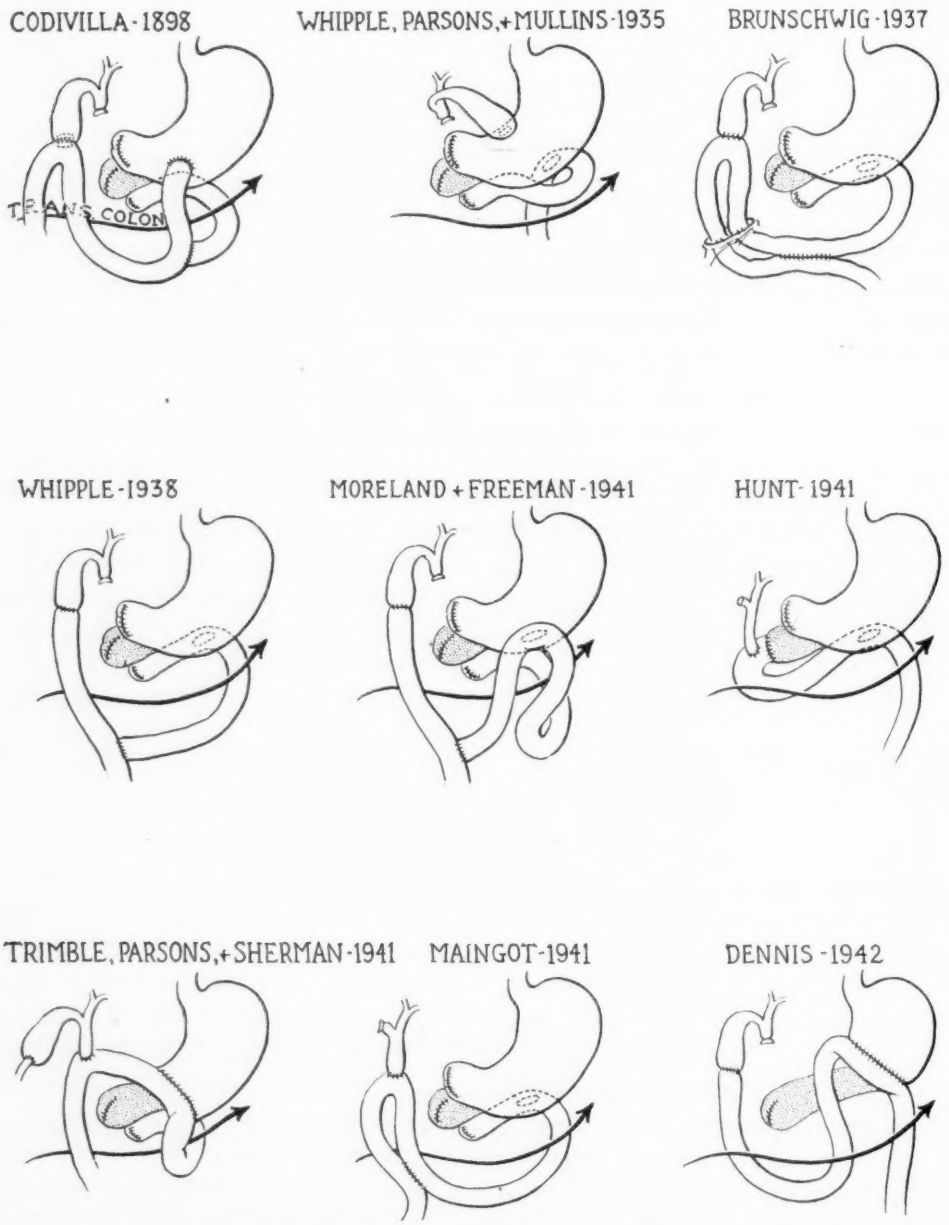

Fig. 1.—Sketches illustrating various techniques of pancreaticoduodenectomy: Codivilla,[10] Whipple, Parsons, and Mullins,[44] Brunschwig,[6] Whipple,[42] Moreland and Freeman,[27] Hunt,[19] Trimble, Parsons, and Sherman,[40] Maingot,[25] and Dennis.[13]

a ligated common duct, (3) location of the anastomoses between the gall tract and pancreas and the jejunum proximal to the gastrojejunostomy to prevent infection of the gall tract and pancreas, (4) anastomosis of the pancreas to the jejunum to prevent pancreatic fistula and to restore the external pancreatic secretion to the intestinal tract. The operations of Whipple,[43] Poth,[35] and Child[9] incorporate these principles (Fig. 3).

COMMENT ON PERSONAL CASES

In addition to the nine cases listed in Table II and Fig. 3, nine other cases have been observed during the period from April 1, 1940, to Nov. 1, 1944. These cases are listed in Table VII.

A study of all diagnoses of carcinoma of the ampullary region brings up the question of the possible operability and curability of such patients. To estimate the value of any operative treatment, it is reasonable to include all

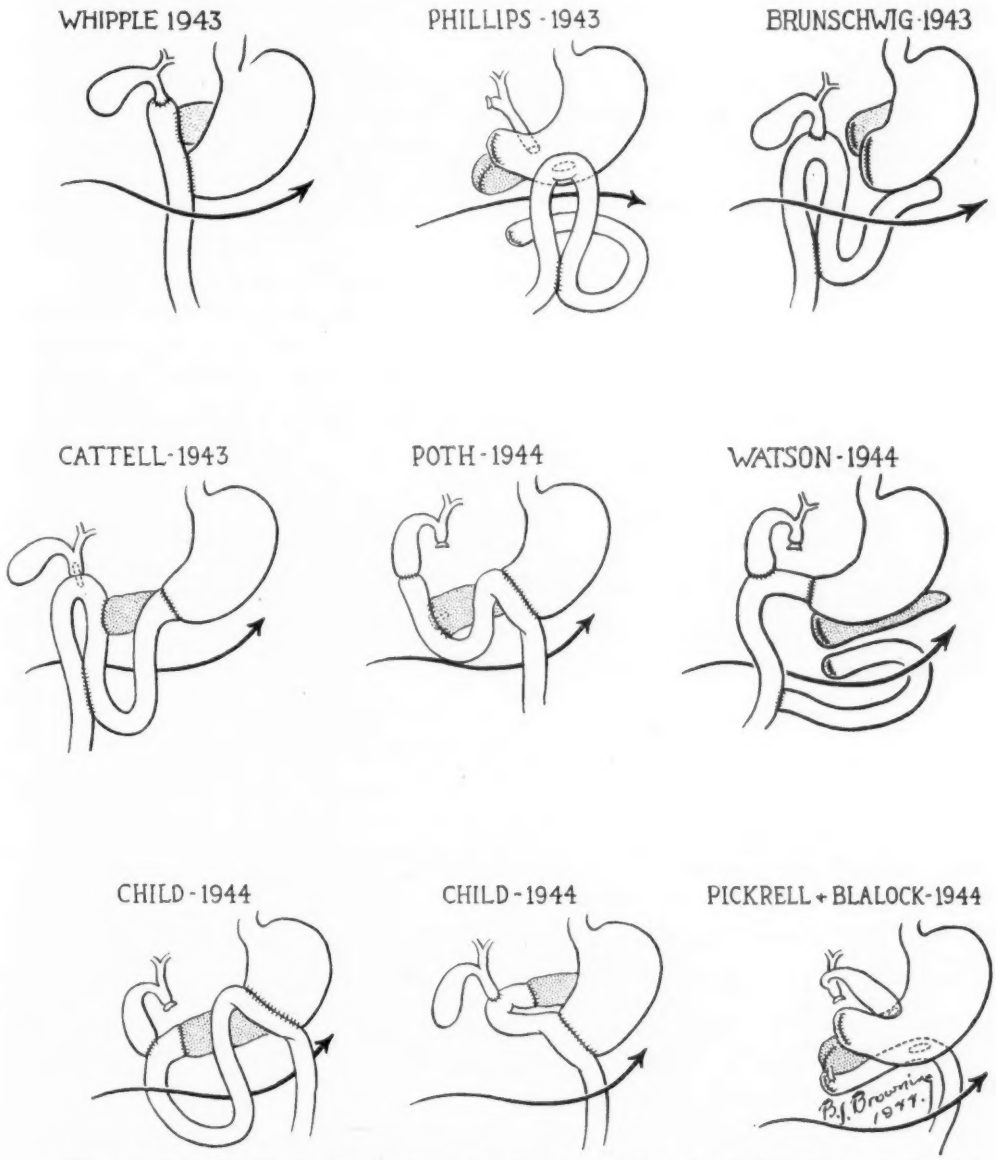

Fig. 2.—Sketches illustrating various techniques of pancreaticoduodenectomy, continued: Whipple,[43] Phillips,[23] Brunschwig,[5] Cattell,[8] Poth,[35] Watson,[41] Child,[9] and Pickrell and Blalock.[34]

patients having the disease. Of the nine patients listed in Table VII, a two-stage pancreaticoduodenectomy was planned for three. Two died following the first stage and one died on the operating table at the beginning of the second stage. Two patients had palliative cholecystogastrostomies because of extensive metastases. A clinical diagnosis only was made in three cases. Operation was recommended in one of these. Carcinoma of the head of the pancreas was found at autopsy in one deeply jaundiced patient who died of advanced pulmonary

tuberculosis. Of the eighteen patients listed in Tables II and VII, eleven had proved metastases or clinical evidence of metastases. The frequency of metastases in this small number of cases makes one wonder just what percentage of such patients is curable by successful pancreaticoduodenectomy.

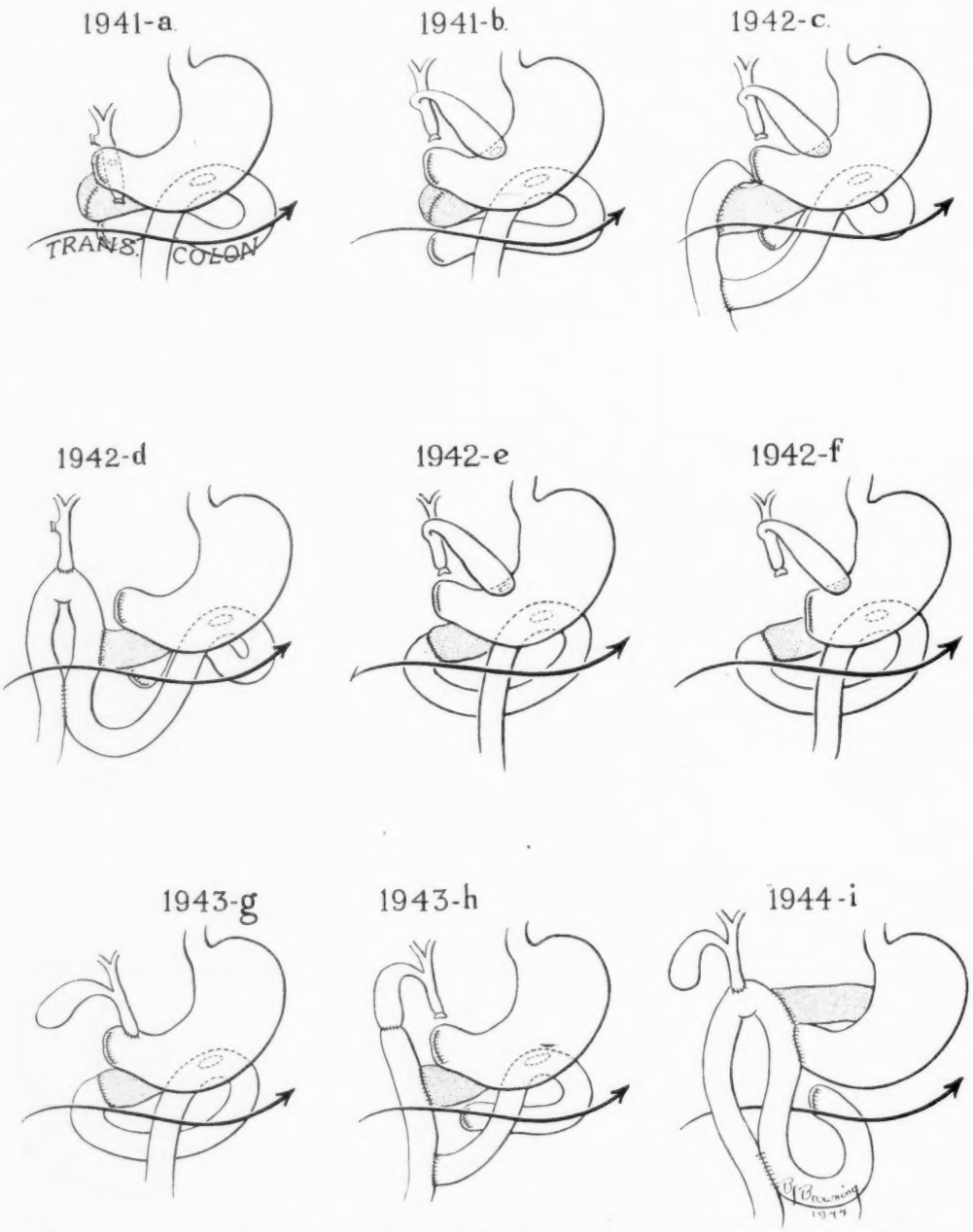

Fig. 3.—Various techniques of pancreaticoduodenectomy used in nine cases in the University of Kansas Hospitals.

CONCLUSIONS

A careful study of each case must be made at the operating table to avoid a needless operation with a high mortality and to select those patients who are considered suitable for a radical operation.

In spite of the rather discouraging results of pancreaticoduodenectomy to date the operation is fundamentally sound and offers the best chance of cure of patients having carcinoma of the ampulla and ampullary region.

The recorded evidence indicates that complete occlusion of the pancreatic ducts will result in fatty infiltration of the liver, reduction in fat and nitrogen absorption in most cases, and fibrosis of the pancreas with atrophy of the acinar tissue. Although there is abundant evidence that patients and animals will live for several years in comparatively good health without the external pancreatic secretion, there has been no valid reason yet recorded why the severed pancreatic stump of pancreaticoduodenectomy should not be united to the intestinal tract. The preservation of the physiology of the pancreas is a very good reason for pancreaticoenterostomy.

The choice of the one-stage or two-stage operation must depend upon the general condition of the patient and the findings at the operating table.

A technique of pancreaticoduodenectomy should be adopted which will reduce the time of operation, minimize ascending infection of the gall tract, prevent pancreatic fistula and biliary fistula, and preserve the normal physiology of digestion.

As in most types of cancer, early diagnosis of carcinoma of the ampullary region is essential to the success of operation. While we cannot credit delay in diagnosis to our medical confreres in all cases, the importance of early diagnosis should be vigorously emphasized and, as Whipple[45] has so aptly remarked, patients with jaundice should not be "studied to death" before they reach the surgeon.

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THE ORIGIN AND GROWTH OF AN ADENOMA OF THE ISLANDS OF LANGERHANS

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STUDIES of the pathology of adenoma of the islands of Langerhans began in 1902, when Nicholls[10] found at autopsy a small tumor of the pancreas; he gave a detailed description of adenoma of the islands of Langerhans based on a careful gross and microscopic study of this tumor. During the next decade similar reports were made by Helmholtz,[4] Morse,[8] Cecil,[2] Heiberg,[3] Rollett,[14] and others, the data for which were obtained at autopsy. A large proportion of the later reports included clinical histories and descriptions of tumors removed surgically. In 1926, Warren[19] suggested the following criteria for the pathologic diagnosis of an adenoma of the islands of Langerhans: (1) that the tumor should be at least 1 mm. in diameter; (2) that the morphology and arrangement of the cells composing the tumor should resemble those of the islands of Langerhans; (3) that the tumor should have a capsule; (4) that the surrounding acinar tissue should be compressed.

Three theories of origin of adenomas of the islands of Langerhans have been proposed. Ssobolew,[17] in 1904, classified a tumorlike structure observed in conjunction with insular hypertrophy as an embryonal rest; Prosorowsky,[13] in 1913, stated the belief that adenomas of the island tissue, like many other tumors, arose from misplaced embryonal germs. Terbrüggen,[18] in 1931, restated the theory of origin from primitive rests. Many investigators accepted the theory advanced by Rollett,[14] in 1912, that adenomas of the islands of Langerhans arose indirectly from the duct system—from islands whose differentiation was not complete. The origin of adenomas of the islands of Langerhans directly from pre-existing mature islands was postulated by Cecil,[2] in 1911, and by Priesel,[12] in 1921. It was the opinion of the latter that cystic adenomas arose from the ducts and solid adenomas arose from the islands. He reiterated Bensley's[1] theory that certain cells in the excretory tubules are totipotent. Hickel and Nordmann,[5] in 1923, in a paper on exocrine adenomas stated the belief that both exocrine and endocrine tumors are derived from the excretory ducts. In one of the tumors described by Smith and Seibel,[16] in 1931, the morphology of the cells, except for the absence of the typical drops of mucin, suggested the possibility of origin from the epithelium of a duct. O'Leary and Womack,[11] in 1934, and Whipple and Frantz,[20] in 1935, supported the view that islet-cell tumors arise from ducts. Accepting this as the most plausible theory, Laidlaw,[6] in 1938, proposed "nesidioblastoma" as a concise, descriptive name, indicative of the origin, to replace the cumbersome and perhaps incorrect term "adenoma of the islands of Langerhans."

The origin and development of the capsule of the nesidioblastoma has received little attention. The presence of a capsule of connective tissue was noted by Nicholls[10] (1902), and the same structure has been reported for many of the tumors described. Elastic fibers were mentioned in reports by Rollett,[14]

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LeComte,[7] Priesel,[12] Schneider,[15] and Natali.[9] Only one author, Warren,[19] specifically mentioned that the capsule of the tumor described by him contained no elastic tissue fibers. An early theory was that pre-existing islands of Langerhans by means of hypertrophy or hyperplasia, or both, encroached upon the less hardy acinar tissue, compressing it and causing atrophy and finally complete destruction of the acinar cells. As the parenchymal cells were destroyed by the steadily growing and advancing tumor, the supporting connective tissue was compressed to form the capsule. The presence or absence of the capsule has been mentioned by various authors, but few of them have reported on any study relative to the capsule or allocated to it any great significance (see Table I). A study of reports of 135 cases, a total of 163 tumors, shows that the capsule was present and complete in 78, incomplete in 25, absent or not mentioned in 60. In the rather wide coverage of the literature, I found no author who suggested that the capsule might be the duct wall, in spite of the fact that many authors stated the belief that adenomas originated from the duct epithelium.

TABLE I. CAPSULE

	NO. OF CASES	NO. TUMORS	CAPSULE PRESENT		CAPSULE NOT REPORTED OR ABSENT
			COMPLETE	INCOMPLETE	
	135	163	77	25	60
Multiple	17	45	16	6	23

The capsule was uniformly complete, incomplete, or absent in all but one of the patients with multiple tumors.

Fig. 1 shows a photomicrograph of a typical adenoma of the islands of Langerhans. The tumor was discovered at autopsy in a man 70 years of age. Symptoms indicated that it had no clinical significance. The adenoma, which was located superficially on the anterocaudal surface of the pancreas, approximately two inches from the splenic end, measured 4.1 by 3.1 by 2.9 mm. The diameter was greatest at the middle, but it was fairly uniform; at each end the tumor was tapered abruptly like the end of a cigar. The entire tumor was sectioned serially, and the sections were variously stained. Staining to bring out the various types of granules was not successful, probably because of improper fixation. The cells of the tumor resembled those of an island of Langerhans. They were cuboidal with a centrally placed nucleus and were arranged in columns and rosettes in close association with numerous blood sinuses and capillaries. The supporting network of connective tissue was heavy. The tumor was surrounded by a complete, rather heavy capsule in which small ducts were visible. Ducts have been noted in capsules by numerous authors. The capsule also contained normal acinar tissue. One can understand the presence of acinar tissue and ducts in the wall of the capsule, as well as the variation in the thickness of the capsule when the entire tumor is studied in serial sections. The outside of the capsule is not smooth like that of a blood vessel, rather it is shaggy and irregular (see Fig. 6). The shaggy, irregular character accounts in part for the variation in the thickness of the capsule and for the presence of acinar tissue and tiny ducts in the capsule. The acinar tissue is not actually embedded in the capsule; a hood of delicate capsular tissue extending from the main capsule embraces but does not surround it. This is diagrammatically illustrated in Fig. 6. If a section were made through the tumor at *X* the capsule would look thick because the top of the hood of capsular tissue would be cut longitudinally. If the tumor were cut at *Y* the capsule would look as if it contained

acinar tissue because to the left there is capsular tissue, then acinar tissue, and finally the lateral embrace of the delicate capsular hood (see Fig. 3, *ac*). As one progresses distally by serial sectioning to a point at *Z*, the filament of capsule embracing the acinar tissue disappears; the acinar tissue has joined the main pancreatic tissue and the capsule looks thin and does not contain acinar tissue. Ducts actually penetrate the heavy capsule. At *D* in Fig. 1, one can see a large duct cut in cross section; it is a typical pancreatic duct. The lining epithelial cells here are somewhat columnar, and the duct contains a secretion

Fig. 1.—Typical adenoma of islands of Langerhans, completely surrounded by a capsule in the wall of which small ducts and acinar tissue may be seen. Note cross section of large pancreatic duct *D*. (Hematoxylin and eosin, ×30.)

possessing staining properties of mucin. As one studies more distal sections of the tumor, a duct, which passes from the main duct, *D*, to the capsule of the adenoma, is seen in longitudinal section (Fig. 3). This also is a typical pancreatic duct. It is interesting to note that this duct enters the capsule of the tumor and courses in its wall for a short distance. The cells lining it are more cuboidal than those of the larger duct. In this section the lumen has just been entered and the wall appears thicker than it actually is. Note the wall in the next section.

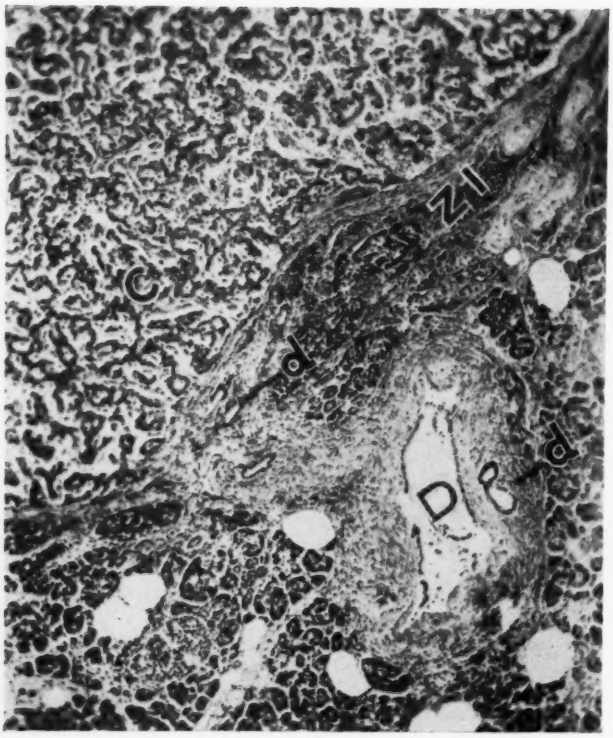

Fig. 2.—More distal section of the same tumor as is shown in Fig. 1; *D*, pancreatic duct in cross section; Z_1, capsule; *C*, tumor cells. Note small ducts (*d*) in the wall of the large pancreatic duct and also in the capsule. (Hematoxylin and eosin, ×75.)

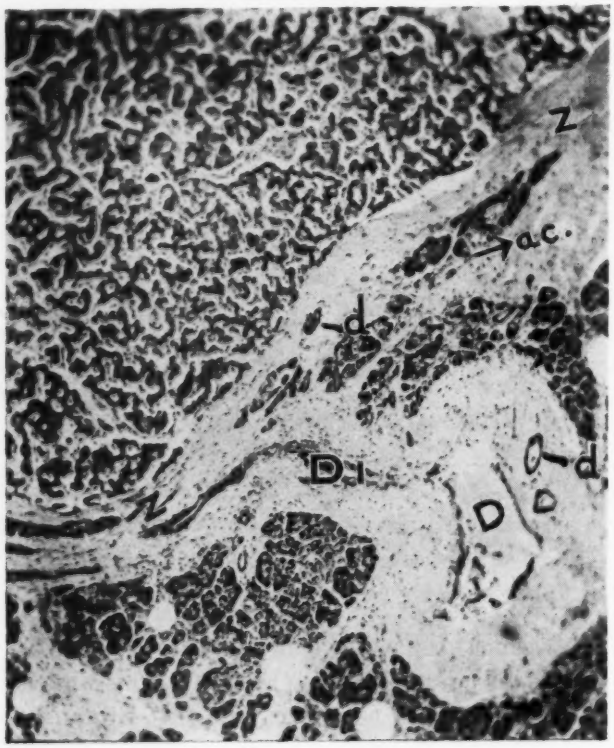

Fig. 3.—Section cut a few microns distal to that shown in Fig. 2. Note the smaller duct (D_1) going from the pancreatic duct *D* to the capsule of the adenoma in which it courses for some distance. Mucin was present in these ducts. The wall looks thick because the microtome had just entered the lumen of duct D_1 in longitudinal section. (Mucicarmin, ×75.)

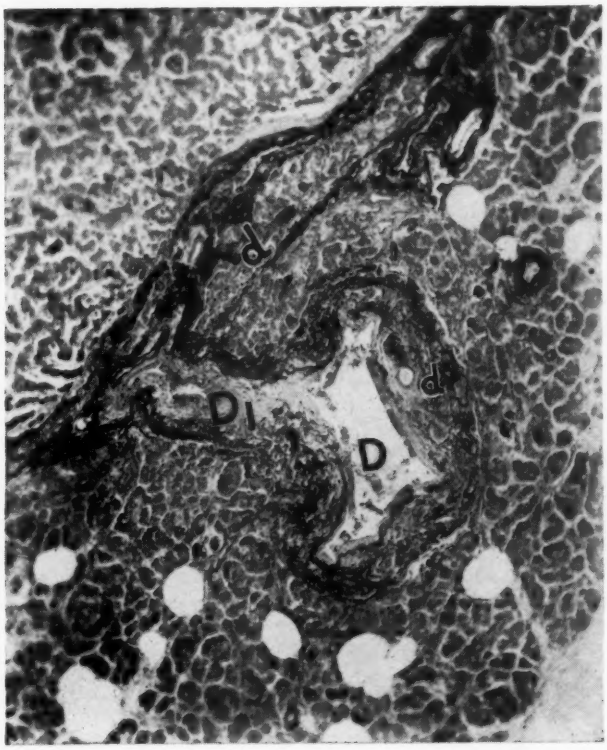

Fig. 4.—A section just distal to that shown in Fig. 3. Generous numbers of wavy elastic tissue fibers can be seen in the wall of the pancreatic duct *D*, cut in cross section, in D_1, the duct cut in longitudinal section, and in the capsule of the adenoma. The architecture of the wall of the duct and of the capsule is the same. Note the absence of elastic tissue fibers in the acinar tissue. (Weigert's stain, ×75.)

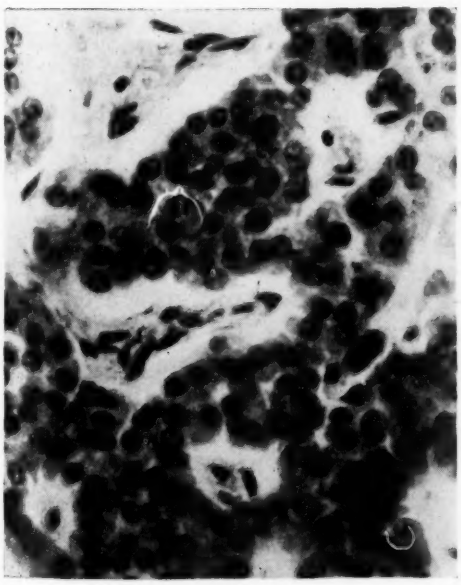

Fig. 5.

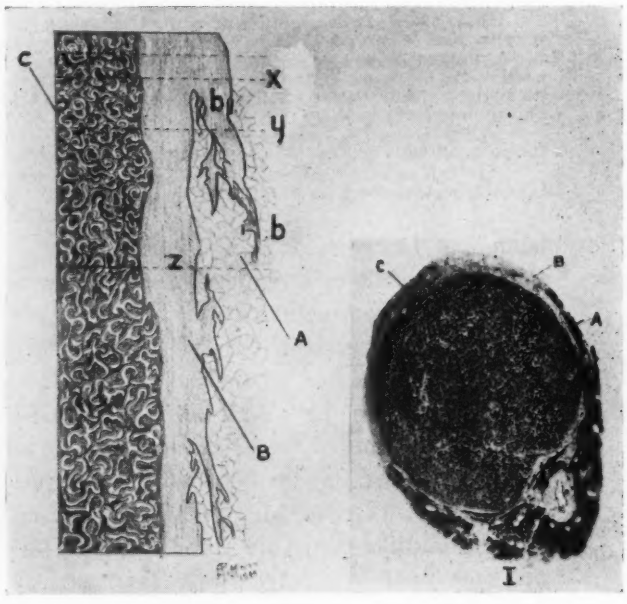

Fig. 6

Fig. 5.—Section showing the tumor cells of the adenoma of the islands of Langerhans. (Hematoxylin and eosin, ×500.)

Fig. 6.—Schematic drawing of a longitudinal section of the capsule of the adenoma. *C*, tumor cells; *B*, the capsule; *A*, acinar tissue. Note the hood or V which *b*-b_1 forms with the capsule and which embraces acinar tissue. A section made at *X* would give the impression of a wide capsule; at *Y* acinar tissue would appear in the capsule (see Fig. 3 *ac*). At *Z* the acinar tissue has joined the main body of acinar tissue.

Insert: Adenoma with capsule in cross section.

Fig. 4 shows a section just distal to that shown in Fig. 3 stained with Weigert's stain. One can see the wavy, elastic tissue fibers interspersed between the collagenous connective tissue elements that form the duct wall. Elastic tissue fibers, which are seen in the cross section of the large duct and in the longitudinal section of the smaller duct, pass into and form a part of the capsule of the adenoma. The capsule itself has a profusion of wavy, elastic tissue fibers. They appear all around the adenoma, wherever the capsule is present. In this single picture one can see that the large pancreatic duct seen in cross section, the smaller duct seen in longitudinal section, and the capsule of the adenoma of the

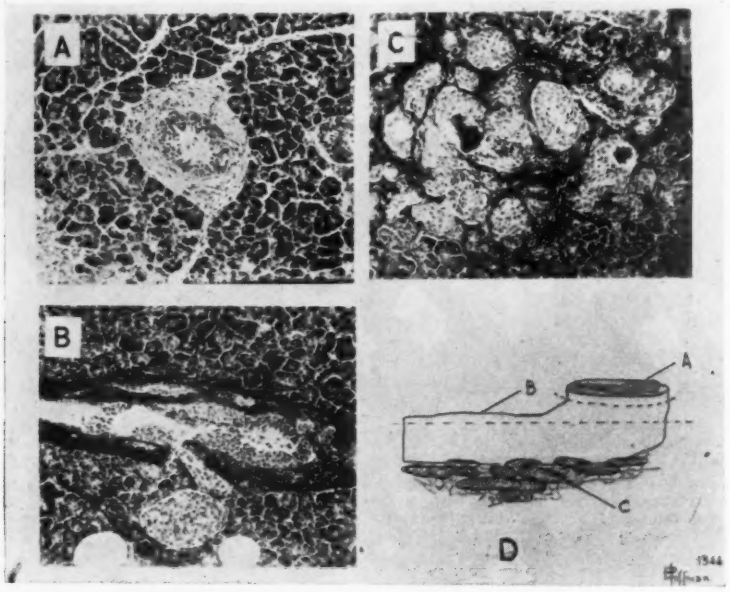

Fig. 7.—*A*, Cross section of a duct, showing proliferation of the duct epithelium. (Hematoxylin and eosin, ×157.)

B, Section 600 μ distal to Fig. 7*A*. Longitudinal section of tributary duct showing connective tissue fibers of the duct wall, proliferation of cells, and a small opening or duct leading through the duct wall; an island of cells having the same characteristics as those of the duct epithelium lies close to the small duct. (Van Gieson, ×157.)

C, Section few microns distal to Fig. 7*B* and just clear of the duct. Many islands of tissue with cells similar to those lining the duct can be seen. (Van Gieson, ×157.)

D, (insert), Schematic drawing showing levels at which sections *A*, *B*, and *C* were taken from the duct and the pancreas.

islands of Langerhans are of the same structure. Consequently, it is my opinion that the capsule of the adenoma of the islands of Langerhans is, in fact, the duct wall. An incomplete capsule can be explained on the basis of overgrowth of the tumor that causes it to break out of the restraining walls of the duct. The presence or absence of the capsule also depends on the point of origin of the adenoma in the duct system (see Fig. 16). If an adenoma originates in the terminal portion of the ducts, the capsule will be absent because there is no wall in this part of the duct system. Illustrations of this type of growth are seen in Figs. 11, 12, and 13. In Fig. 12 one can see a small duct connected with a large islandlike structure from which it, no doubt, took its origin. Many islands are seen near by. Seventy-five per cent of the multiple tumors occur in close proximity. Twenty-five per cent are found in widely separated segments of the pancreas. It should be noted that the duct has no wall. Fig. 13 shows an enlarged island, 1 mm. in diameter, that fulfills the earlier criteria for diagnosis of an adenoma of the islands of Langerhans except that it has no capsule. The absence of a capsule can be explained on the basis that the proliferation began in the duct system where the wall is absent.

Few examples of adenomas in the process of growing or of duct epithelium in a state of proliferation have been reported in the literature. Parts *A*, *B*, and *C* of Fig. 7 show photomicrographs of duct epithelium in a state of proliferation. Fig. 7, *A*, is a cross section of a duct. Note the proliferation of the duct epithelium. In the section shown in Fig. 7, *B*, 600 μ from that in Fig. 7, *A*, the lumen of

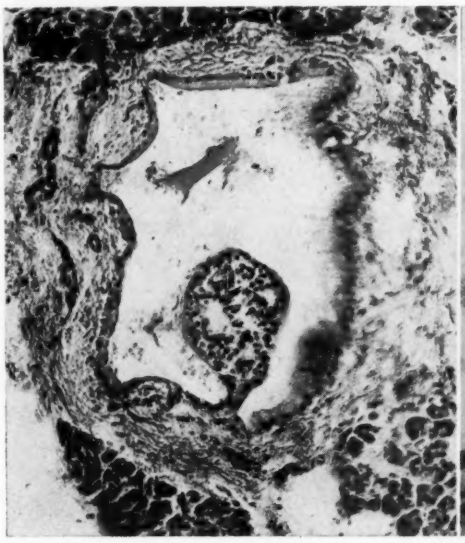

Fig. 8.

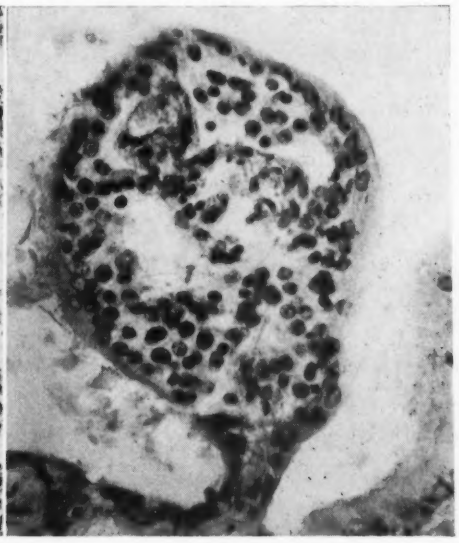

Fig. 9.

Fig. 8.—An unusual specimen. The section shows a polyp of islandlike structure growing directly into the lumen of a duct, originating from the duct epithelium. It is easy to conceive that the polyp would grow, fill the duct, and expand into an adenoma. Note the shape of the duct in cross section. (Hematoxylin and eosin, ×150.)

Fig. 9.—The same section enlarged to show the similarity of the cells to those of an island of Langerhans. (Hematoxylin and eosin, ×500.)

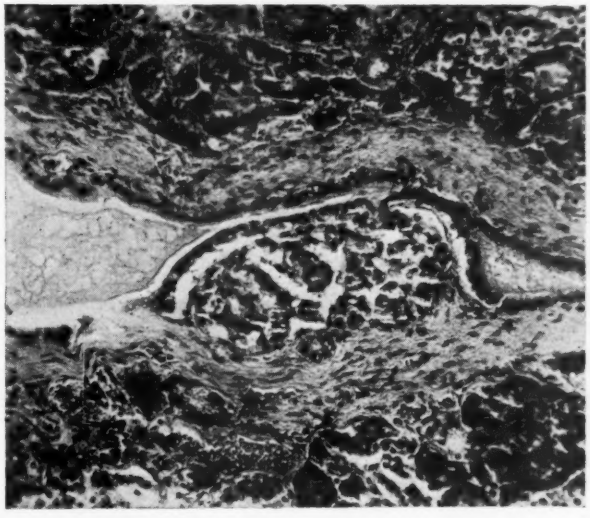

Fig. 10.—Another unusual specimen. Note the growth of the duct epithelium; it has practically occluded the lumen of the duct and is now the size of an average normal island of Langerhans. (Hematoxylin and eosin, ×157.)

the same or a tributary duct running at right angles to this was cut longitudinally. The proliferation of the epithelium is still evident and a small tributary duct enters at this level. The same type of proliferation and the same type of cells appear in the tributary and in the large duct. A section made just distal to

the duct is shown in Fig. 7, *C*. There are many islands of cells separated by heavy supporting connective tissue. The cells composing these islands resemble those which were proliferating in the adjacent duct. Fig. 7, *D* shows the levels from which sections *A*, *B*, and *C* were taken.

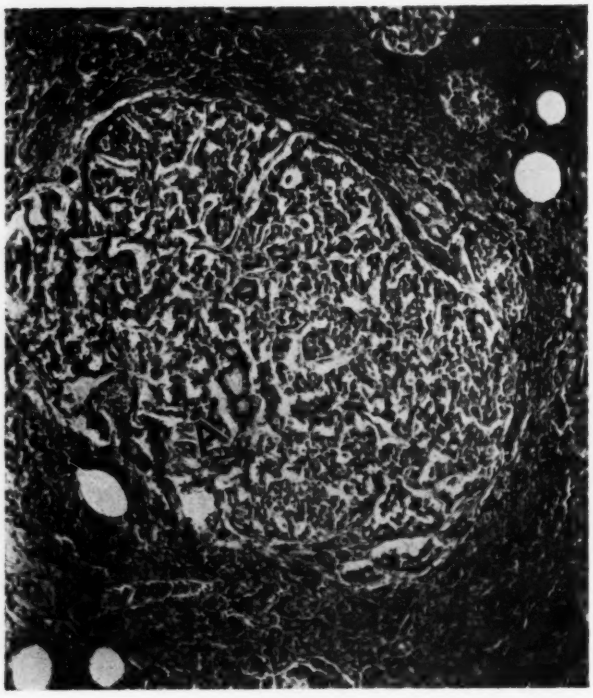

Fig. 11.

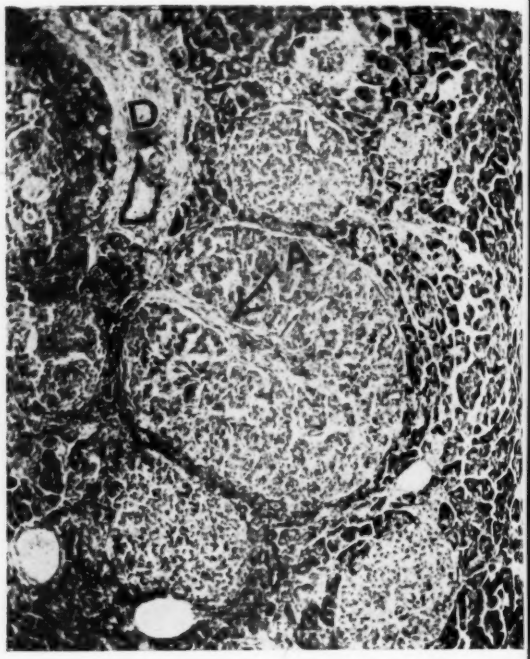

Fig. 12.

Fig. 11.—This isletlike structure measures 1 mm. The acinar tissue surrounding it is compressed. There is no capsule, and a duct, *A*, seen at the center has no wall. (Hematoxylin and eosin, ×75.)

Fig. 12.—Section showing a large island with a small duct, *A*, coursing almost to the center of the island. This duct seems to be a tributary of the larger duct *D*. Note islands near by. (Hematoxylin and eosin, ×75.)

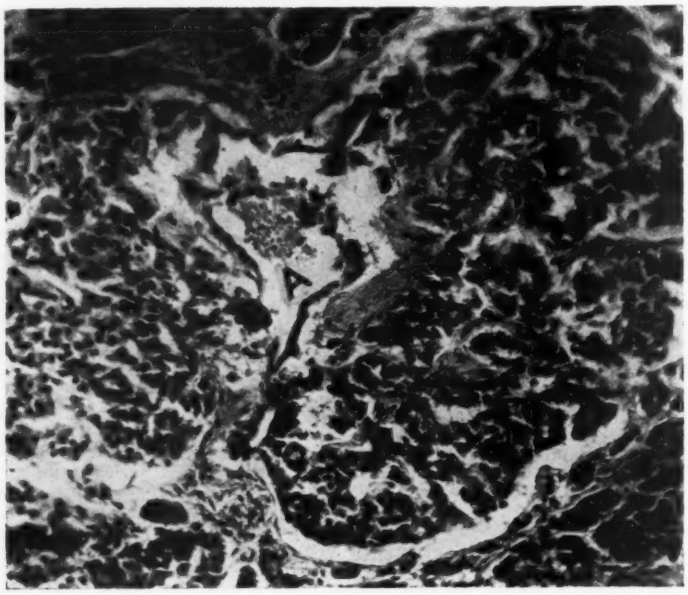

Fig. 13.—Section through an island (1 mm. with a duct, *A*, in its center. (Hematoxylin and eosin, ×75.)

As uncommon as are reports and photomicrographs of proliferating epithelium of the ducts, illustrations or descriptions of an adenoma in the stages of growth are still rarer. I obtained some photomicrographs of rare specimens which I believe can be considered as demonstrating stages in the growth of an adenoma. Figs. 14 and 15 also show proliferating duct epithelium which almost fills the lumen of a duct and the mass of cells measures about 200 μ.

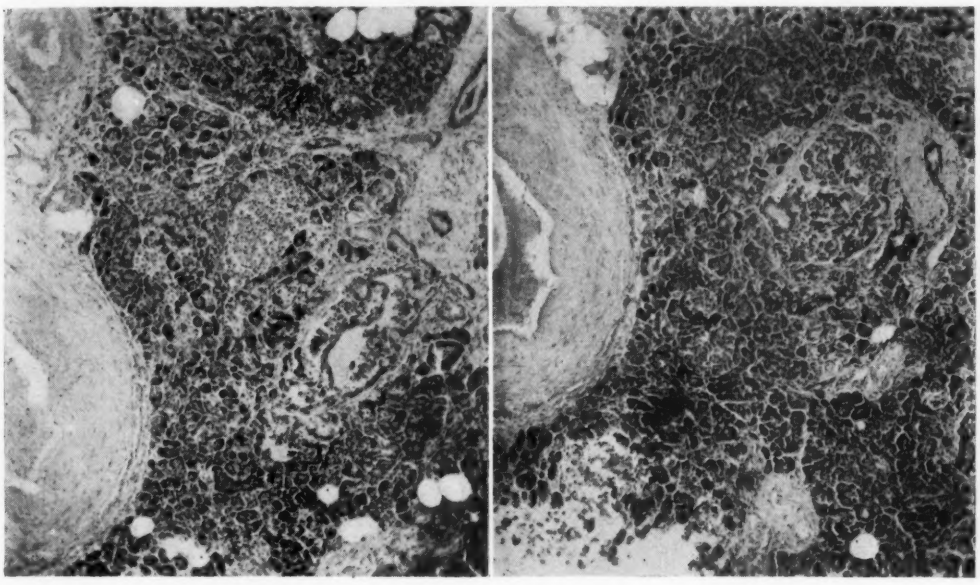

Fig. 14. Fig. 15.

Fig. 14.—Longitudinal section through a pancreatic duct showing proliferation of epithelium. (Hematoxylin and eosin, ×75.)

Fig. 15.—Same specimen 200 μ distal. Mass of cells resembles islands of Langerhans in size and appearance. (Hematoxylin and eosin, ×75.)

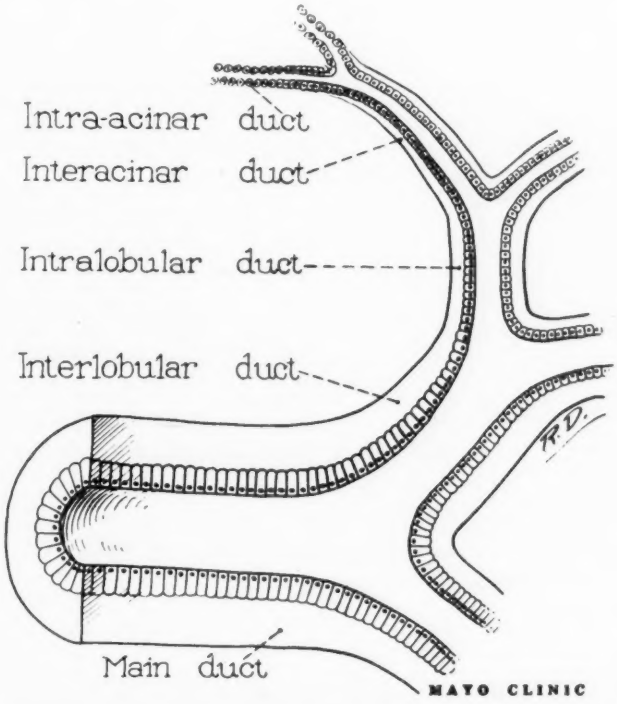

Fig. 16.—Schematic drawing of the duct system. Ducts usually branch at right angles rather than as shown. Terminal ducts show no wall.

Please note that the length of the proliferating mass is a little greater than the diameter of the duct in which it has taken origin.

Fig. 10 presents another unusual specimen. The growth of the duct epithelium has almost occluded the lumen of the duct and is now almost the size

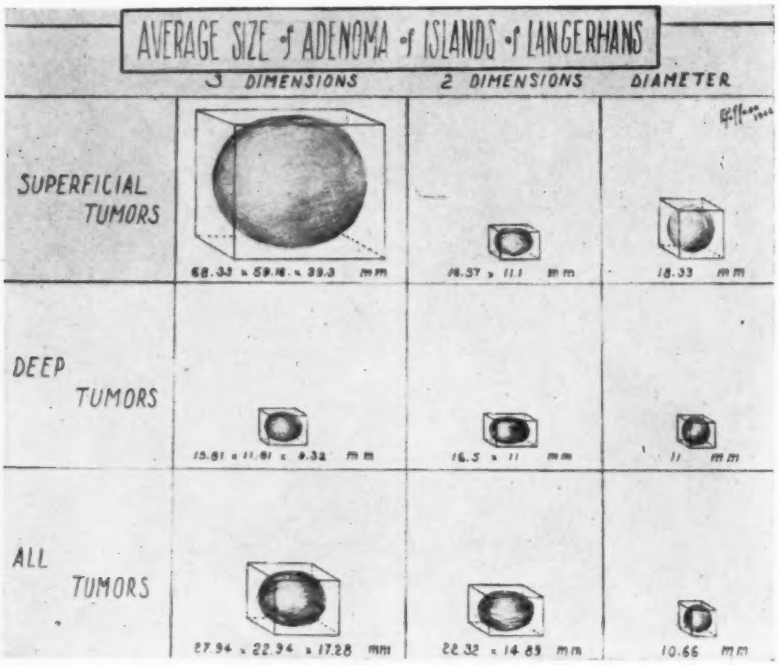

Fig. 17.—Schematic representation of the average size of adenomas of the islands as reported in literature. Some authors gave measurements in three and some in two dimensions, some in diameter only. Averages for each method are recorded and drawn to scale.

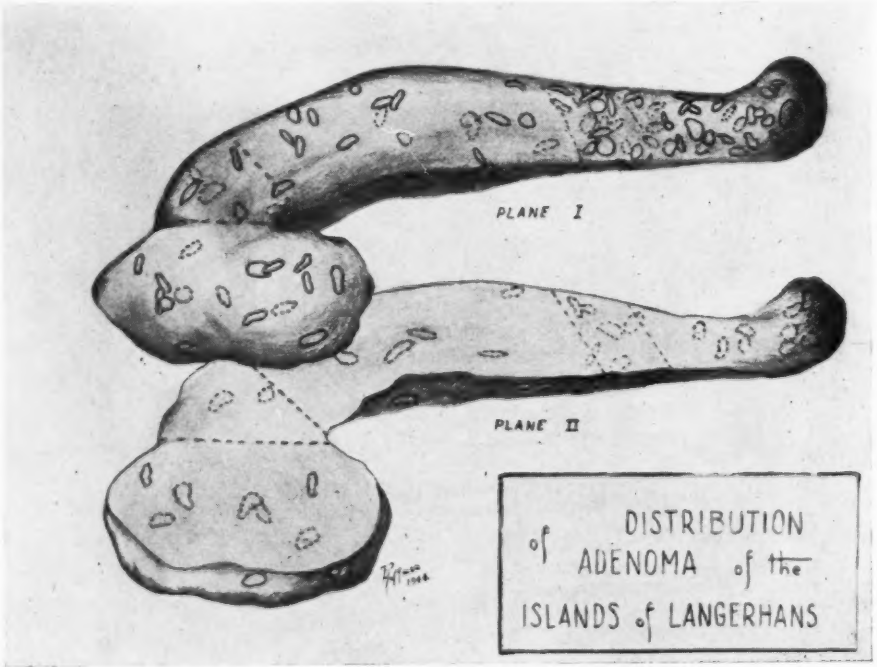

Fig. 18.—Distribution of adenomas reported in the literature. The pancreas has been sectioned sagittally. The superficial tumors are represented in the anterior, the deep in the posterior, section.

of a normal island (240 μ). The proliferation seems to have taken place subepithelially and has pushed the lining epithelium, unbroken, in front of the advancing mass of cells. It is easy to see how, with continued proliferation of cells, the lumen of the duct would be filled and an adenomatous mass would be formed with the duct wall as its capsule. It is also easy to see that the growth would take place with less resistance along the lumen than against the wall; and if this is true, theoretically the length of an adenoma arising in a walled duct would be greater than its cross diameter. The reports of authors who have carefully measured the size of the tumors in three dimensions substantiate this theory (see Table II and Fig. 17).

Fig. 8 shows an unusual specimen—a polyp of islandlike cells arising from the duct epithelium and growing directly into the lumen of the duct. The polyp measures ⅓ by ¼ mm. Fig. 9 shows this polyp under high power to illustrate the great similarity of the cells to those of an island of Langerhans. It is easy to imagine that this polyp could grow, fill the duct, expand into an adenoma, and become surrounded by a capsule or the duct wall. The duct measures 0.8 by 0.7 mm. in cross section, and the shape corresponds roughly to the outline of an average adenoma.

While not strictly within the limits of the subject matter of this paper, there are facts closely enough related to the growth of the adenomas to be permissible for inclusion in the paper, and which, at the same time, I believe will lend considerable interest for surgeons. Of the 135 cases of adenoma reported

TABLE II. AVERAGE SIZE IN MILLIMETERS

TUMORS SITUATED	THREE DIMENSIONS	TWO DIMENSIONS	DIAMETER
Superficially	68 × 59 × 39	16.5 × 11	18
Deep	16 × 12 × 9	16 × 11	11
All (including those whose location was not stated)	28 × 23 × 17	22 × 15	11

in the literature, in 17 cases, or about 8 per cent, multiple adenomas were present. Surgeons must recognize that in 1 of every 10 cases of hyperinsulinism due to adenoma, the tumor will be multiple. In 75 per cent of these cases, the tumors will be found in fairly close proximity to each other; in 25 per cent, the tumors will be found in widely separated areas. The character and pattern of the multiple tumors are very much alike. For example, the capsule was complete, incomplete, or absent, uniformly in all cases of multiple tumors with the exception of one. The distribution of the tumors is diagrammatically shown in Fig. 18. The superficial tumors are presented in the anterior sagittal section; the deep tumors are drawn in the posterior sagittal section. Tumors which were definitely localized are drawn accordingly in the diagram as to position, but not as to size. Many are not accurately described and had to be distributed on the basis of inaccurate knowledge. Table III gives the available data collected from the literature. As one would expect from a knowledge of the distribution of the islets of Langerhans, the tumors predominate in the tail of the pancreas. Tumors which are found in the tail are superficially located in a great majority of the cases. In the head, the majority of the tumors are found deep in the pancreatic tissue. It has occurred to me that the terminal (peripheral) blind-end ducts were more likely to be the seat of adenomas. If so, the interlocking ducts between the dorsal and ventral pancreases might offer an explanation for the predominance of the deep-seated tumors of the head and neck of the pancreas.

TABLE III. LOCATION OF ADENOMA OF ISLANDS OF LANGERHANS

TUMORS	HEAD	JUNCTION HEAD AND BODY	BODY	JUNCTION BODY AND TAIL	TAIL	EXTRA PANCREATIC	NOT LOCALIZED	TOTAL
Number	21	8	18	16	34	6	60	163
Multiple	7		10		11			
Combined	4		2		2			

A drawing has been made to show the relationship in size which exists in tumors found superficially and deeply. Some authors (as they should) measured the tumors in three dimensions, others in two dimensions, and finally, some gave only the diameter. Consequently, in Table II is shown the average size of the adenoma based upon each of the several ways of measuring. Tumors described with comparative sizes were not included. The average size of the superficially placed adenoma measured in three dimensions is four times the size of a similarly deeply placed tumor. The large size of the superficial may be due to an erroneous inclusion of a low-grade malignant adenoma. In general, the superficially placed tumors are larger than those located deep in the pancreatic tissue. There is less resistance to growth. The measurement of tumors in three dimensions shows that the tumors are definitely elongated and that the diameter of a cross section of the tumor shows it somewhat flattened. See shape of duct, Fig. 8.

SUMMARY

An effort has been made to show that the structure of the wall of the pancreatic duct and the wall of the capsule is the same, and, therefore, the capsule is the duct wall and its presence or absence depends upon whether the adenoma took origin in a duct with or without a wall. And finally, the gulf which exists between the theory of origin and a mature adenoma has been bridged by showing the proliferation of the duct epithelium, and intraductal islands of cells representing stages of growth.

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ISLET-CELL TUMORS OF THE PANCREAS

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THE relationship of certain islet-cell tumors of the pancreas to hypoglycemia is now well recognized and interest in this regard has been demonstrated by the increasing number of cases reported in the literature in the last decade. Islet-cell tumors of the pancreas generally conform to the conception of hyperinsulinism which was formulated by Seale Harris. There are generally signs of insulin shock of varying degree with an abnormally low blood sugar level, the symptoms in most instances being relieved by the ingestion of carbohydrate.

The first islet-cell tumor was reported by Nicholls, in 1902, who found a simple adenoma of the pancreas arising from the islands of Langerhans. Later, in 1926, Warren, in reviewing the literature, was able to find only sixteen cases of adenoma but he was able to add four of his own. None of these tumors presented any symptomatology or clinical signs which would have led to their discovery and, as a result, the conclusion drawn was that they were only of academic interest.

The discovery of insulin in 1922, by Banting and Best, was followed by the recognition of insulin shock. In 1924, Seale Harris, observing similar reactions in a limited number of cases, conceived the possibility that hyperinsulinism and hypoglycemia might occur as a result of oversecretion on the part of either hyperplastic islets or tumor of the islands of Langerhans. At this time, however, he called attention to other glands of internal secretion whose action might influence hypoglycemia, such as the thyroid, the anterior lobe of the pituitary, and the adrenals.

The first case showing true evidence of hypoglycemia and hyperinsulinism was reported by Wilder and his associates. In this patient there was a typical picture of insulin shock which failed to respond adequately to the ingestion of carbohydrates. At operation, at a later date, a carcinoma involving the islands of Langerhans was found with metastasis to the liver. Later at necropsy, an essay of the metastasis showed a definite insulin content. Following this, case reports were made by Thalheimer and Murphy, McClenahan and Norris,

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and others. The first islet-cell tumor giving typical signs of hypoglycemia with hyperinsulinism diagnosed and treated successfully by surgery was reported by Howland and his associates. This patient showed an adenoma. Its removal was followed by complete recovery and subsidence of all symptoms. Whipple, in a recent review, was able to report 149 islet-cell tumors showing hypoglycemia. Of these, 106 were considered benign, 28 questionably malignant, and 15 definitely malignant with metastases to the liver.

These tumors are generally single but two or more have been found in approximately 10 per cent of the reported cases, being located principally in the body and tail of the pancreas but they may be found in the head of the gland. In situ these tumors are dark red or purplish in color due to increased vascularity and are firmer than the surrounding tissues. Their size varies but the average is 1 to 2 cm. in diameter. The tumors which are benign are encapsulated as are some of questionable malignancy. They may show signs of degeneration, either hyaline or fibrous, and in some cases are definitely calcified. On microscopic section the cells are typical of islet cells, being edematous, but vary in arrangement and differentiation. In the questionably malignant group there is some congestion of the capsule, and islet cells may be found in the capillary beds. Alpha and beta cells may be demonstrated by special staining.

The symptoms of islet-cell tumor may be hunger, sensation of faintness, perspiration, and vertigo or there may be signs in addition which are related to the nervous system. Wilder has classified the nervous symptoms under three groups: (1) disturbance of the sympathetic nervous system with dizziness, nausea, pallor, and sweating; (2) disturbance of the central nervous system, such as convulsions with tonic and clonic contractures of the extremities; (3) psychic disturbance with anorexia, maniacal seizures, mental confusion, and coma. These attacks frequently occur during periods of fasting or overfatigue, at which time the blood sugar levels are low. There is frequently a rapid response to the ingestion of glucose either by mouth or parenterally.

Whipple has presented a triad which he believes is very useful in differentiating possible islet-cell tumors: (1) attacks of insulin shock coming on during fasting or an overfatigued state; (2) blood sugar findings of 50 mg. per cent or less; (3) prompt relief by the ingestion of glucose. When this triad is present the possibility of islet-cell tumor due to an oversupply of insulin must be seriously considered.

The presence of hypoglycemia presents a diagnostic problem. The influence of the other glands of internal secretion affecting carbohydrate metabolism must be given careful attention. The thyroid can be ruled out frequently by the clinical picture with the findings of dysfunction of the gland including an abnormal basal metabolic rate. In the case of the pituitary, x-ray picture of the skull should show a widening or destruction of the sella turcica, and the presence of headaches with visual disturbance would indicate the presence of a tumor in this region. In the case of the adrenals, we might expect Addison's disease or findings of adrenal tumor itself. The liver, too, should be carefully considered but these cases show evidence of liver damage or insufficiency, the patient manifesting symptoms of acute illness. The glucose tolerance test does not always give evidence which may indicate the definite presence of islet-cell tumors; even the use of alloxan offers no positive aid in diagnosis.

The medical treatment of hyperinsulinism due to suspected islet tumor is avoidance of fatigue and overexertion, and the intake of large quantities of glu-

cose either by ingestion or injection. Mild cases may be benefited and surgery delayed or avoided.

Surgery must be employed in those more severely ill patients who are not adequately responsive to palliative measures. The general condition of the patient should be brought to the best possible level by a high protein, high carbohydrate intake supplemented by plasma and blood transfusions.

The transverse or inverted T incision is particularly suited to operations on the pancreas. The gland may be approached through the gastrohepatic or gastrocolic omentum but in either instance exposure should be adequate. If most of the greater curvature of the stomach is freed and reflected upward, practically the entire anterior surface of the pancreas can be visualized. Islet tumors may be quite obvious or not visible at all and in the latter instance the entire gland should be carefully palpated. In the presence of an obvious adenoma its removal is usually adequate to accomplish a complete relief of symptoms. However, it must be borne in mind that these masses may be multiple, and additional tumors should be removed when present. Several instances are reported in which a patient has required a second operation for removal of an adenoma missed at the first operation. What procedure to employ when a tumor cannot be found is open to debate. The abdomen may be closed and further observation awaited to perform a possible second operation when the tumor is sufficiently developed to permit its location and removal, or an adequate portion of the pancreas may be resected with the idea of cutting down the secretion of insulin similar to the treatment of hyperthyroidism, in the hope that the removed segment of gland may bear the offending tumor. In view of the fact that islet tumors usually invade the body and tail of the pancreas, this is the portion removed. Bruschwig stated concisely that in those patients presenting the essential triad, an exploratory laparotomy is indicated for excision of pancreatic islet-cell adenoma or, failing to find this, a subtotal pancreatectomy should be performed. This advice is also subscribed to by David, Cole, and others. According to David, approximately four-fifths of the gland lying to the left of the mesenteric vessels and weighing about 48 to 72 Gm. should be removed. To facilitate the operation and to guard against hemorrhage Whipple recommended ligation of the splenic vessels and splenectomy. Drainage must be employed to carry off leakage from the cut surface of the pancreas. This secretion, however, is not unduly irritating to the skin as the digestive ferments have not been activated. Holman and his co-workers have reported a number of cases in which extrapancreatic islet adenomas have been the cause of hyperinsulinism and hypoglycemia.

CASE REPORT

Mr. K. M., aged 24 years, whose family history and past history are of no importance, was a discharged soldier from the present world conflict. He was wounded twice in service, from which he recovered in a comparatively short time and was returned to regular infantry duty. He experienced the first symptoms when he became unconscious while on sentry duty. Because of these attacks of unconsciousness he was sent to a hospital and evacuated to the United States. He experienced several attacks during the process of evacuation. In the United States he was studied in army hospitals but no definite diagnosis was arrived at and he was finally discharged as an epileptic.

The patient was sent to the Veterans Hospital for further study and diagnosis. During the examinations it was noted that it was difficult to arouse him in the morning, that he experienced lethargy, drowsiness, and irritability, and was most uncooperative and difficult to manage, so much so that it was necessary to keep him in a lock section. Repeated blood sugar examinations were persistently low and on several occasions the patient went into a deep stupor at which time the blood sugar was found to be as low as 45 mg. per cent. He

went A.W.O.L. from the hospital, was gone two days without medical attention, and was returned by ambulance to the hospital in a state of coma. The blood sugar was found to be 28 mg. per cent. He promptly regained consciousness following the administration of glucose both intravenously and orally. Thorough study revealed the patitent to be hypoglycemic, typical of hyperinsulinism, fulfilling the essential triad of Whipple for islet-cell tumors of the pancreas.

The patient was operated upon under continuous spinal anesthesia, Feb. 28, 1944, after a thorough preoperative preparation. A transverse incision was made first but this was not adequate for ready access to the pancreas and an inverted T incision was then carried upward in the midline. This afforded adequate exposure. The gastrocolic omentum was divided, the stomach retracted upward, and the transverse colon downward. The pancreas was exposed throughout almost its entire length. No islet tumors could be visualized or palpated by means of a most meticulous examination. As a result, approximately 75 per cent of the pancreas, namely that portion to the left of the superior mesenteric vessels, was completely dissected free by doubly clamping all vessels and immediately ligating each clamped vessel. There was an unusually small amount of hemorrhage and the pancreas was doubly clamped and divided. The proximal end of the pancreas was closed by mattress sutures of chromic catgut. The abdomen was closed with a cigarette drain placed at the cut off stump of the pancreas. Primary healing ensued and the patient made a splendid recovery.

Following operation the blood sugar mounted and it became necessary to give a few hypodermics of insulin. Later it became stabilized and has run persistently about 100 mg. per cent.

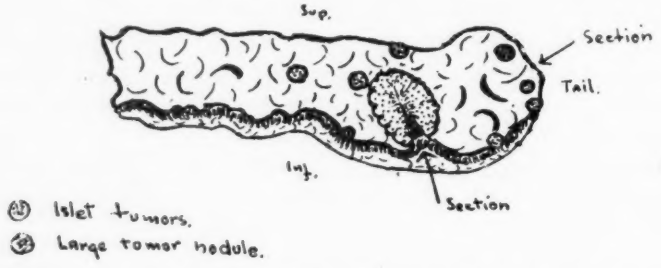

Fig. 1.—Left two-thirds of the pancreas with one primary active islet adenoma and eight addftional inactive adenomas, schematic.

Since his operation I believe one is justified in calling this patient cured inasmuch as he has had no more attacks of coma, he has had a gradual but progressive return of weight and strength, he has a stabilized, normal blood sugar, and a complete reversal of personality. It is most interesting indeed to note that this young man, so difficult and uncooperative, has become a pleasing, attractive individual.

Histopathologic Report.—

Gross specimen: The specimen was an elongated portion of firm ocher-colored lobulated tissue measuring 14 by 4 by 2 cm., weighing 46 Gm., and said to be an excised portion of the pancreatic gland. The specimen was received incised and revealed a small, dark nodular mass measuring 0.8 cm. in diameter. This portion was situated in the tail end of the pancreas.

Serial sections through the pancreatic tissue, approximately 0.5 cm. apart, revealed similar small nodular masses scattered throughout the tail end of the specimen. The largest mass measured 1.2 cm. in diameter, was hemorrhagic in character, and sharply defined from the adjoining pancreatic parenchyma.

Microscopic description: Section through the pancreas at the site of the grossly described incised nodular mass revealed the normal pancreatic architecture to be disrupted and replaced by a well-demarcated mass of pink- and lavender-staining amorphous material containing numerous cellular aggregations corresponding to islet tissue. Its line of demarcation from the normal adjoining pancreatic parenchyma was sharp and the adjacent adipose tissue was densely infiltrated with red blood cells.

Another section revealed a prominent accumulation of pale-staining cellular elements sharply demarcated from the surrounding parenchyma. These cellular elements had a clear cytoplasmic structure with prominent hyperchromatic nuclei. The nuclei showed no variation in size and shape. Although within some regions the nuclear structures had a tendency to·

ward palisading, there was insufficient evidence to warrant a diagnosis of malignant change. Within the same region small acinar structures were ascertainable, filled with pink-staining homogeneous material. The interstices of these acini contained accumulations of frank blood.

Another sharply demarcated accumulation was found almost immediately adjacent to the previously described structure. This tissue, however, in no way resembled the latter but consisted primarily of trabeculated strands of hyperchromatic nucleated structures enmeshed in a matrix of pink- and lavender-staining fibrinous material. As compared to the cellular elements of the previously described nodule, these cells revealed marked eosinophilic granulated cytoplasms and a definite variation in size and shape. Several areas within this accumulation appeared to be undergoing active degeneration. Careful study revealed no evidence of acinar formation.

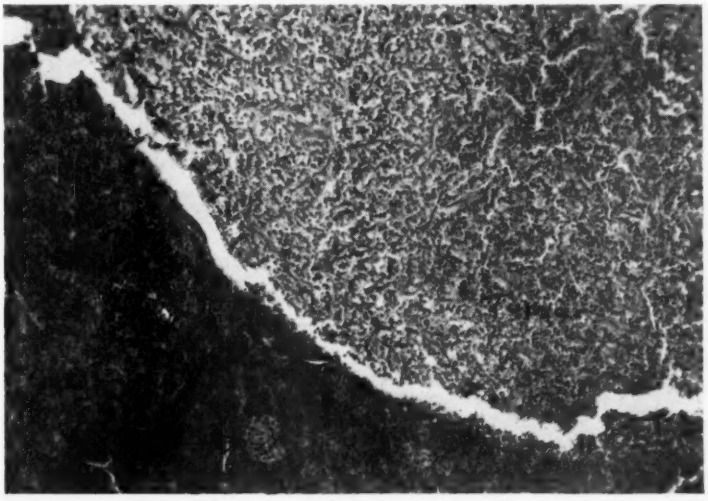

Fig. 2.—Normal islet-cell cluster in the normal pancreas. Line of demarcation between the islet-cell tumor and normal pancreatic gland. There is a distinct similarity of tissue in both the islet-cell tumor and the normal gland.

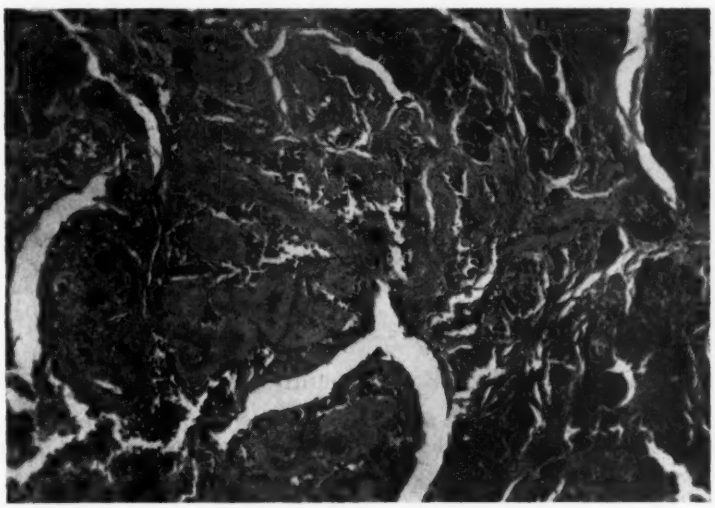

Fig. 3.—This section of the islet-cell tumor displays the variable amounts of hyaline and cystic degeneration which displaces islet cells, similar to that seen in thyroid adenomas.

Within the same section were nine distinct nodular masses presenting characteristic evidences of hyperplasia of the islet tissue of the pancreas. However, of these nine nodular masses only one presented a characteristic solid clear cell accumulation which has been classically described as an islet-cell tumor. The cellular elements of the latter nodular accumulation showed a predominant basophilic granulation through the cytoplasmic structures.

In addition, the nuclei did not contain as much chromatin as the nodular masses previously described.

CONCLUSIONS

1. The clinician must be on the alert for that triad of symptoms described by Whipple which indicates the presence of an islet-cell tumor of the pancreas.

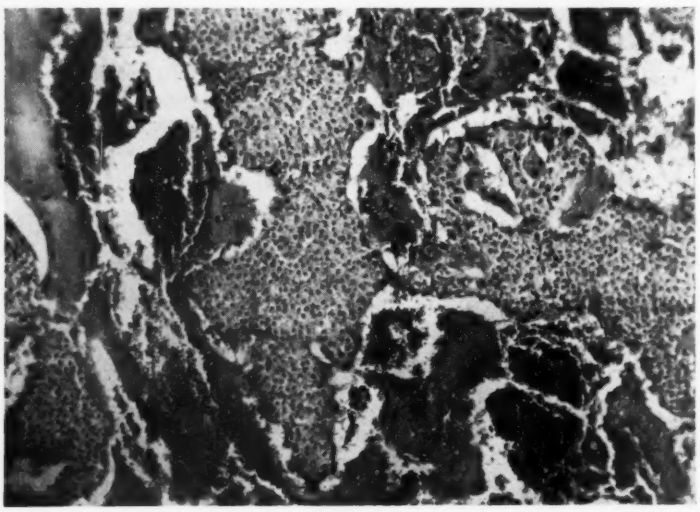

Fig. 4.—High-power view showing characteristic islet tumor cells.

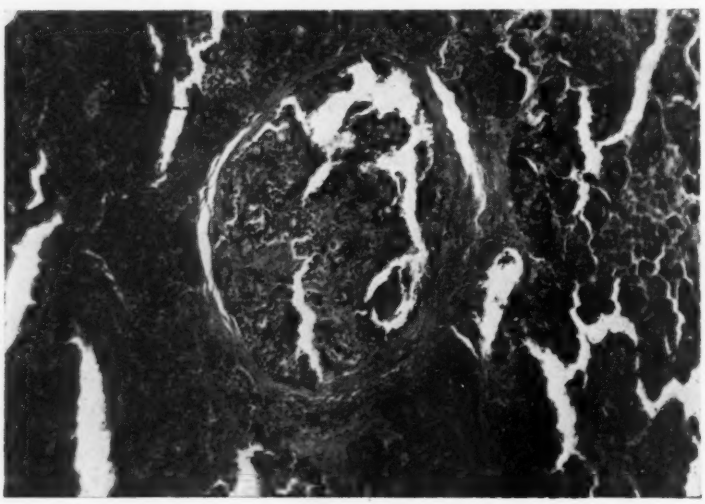

Fig. 5.—An islet tumor about twenty times the size of the normal islet seen in the normal surrounding pancreas.

2. When this triad is present, an operation exploring the pancreas is indicated.

3. Removal of an obvious islet-cell tumor or tumors should be performed. When these cannot be visualized, pancreatic resection may be advisable. The present case report substantiates the latter statement inasmuch as nine islet tumors were found in a pancreas when they could not be demonstrated by vision or by palpation.

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GASTROJEJUNOCOLIC FISTULA

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DURING the ten-year period from 1934 to 1944, forty-seven patients were treated by surgical operation for marginal or jejunal ulcer at the University of Michigan Hospital. Five of these forty-seven patients required an additional operation during this same period because of recurrent gastrojejunal ulceration and one patient was operated upon three times for this same condition. Thus, a total of fifty-four operations was performed upon forty-seven patients. Of the afore-mentioned forty-seven patients, eight or 17 per cent had the serious complication of gastrojejunocolic fistula. It is with this latter group of cases that the present discussion is concerned. This incidence of 17 per cent is slightly lower than that reported by Benedict[1] at the Massachusetts General Hospital, who found the incidence of fistula due to perforation of jejunal ulcer into the colon to be 23.8 per cent in twenty-one patients with jejunal ulcer treated surgically. However, when all of his marginal ulcer cases were considered, that is, those treated both medically and surgically, the incidence of fistula was found to be 13.9 per cent. According to a report by Verbrugge,[2] the incidence of fistula was 11.36 per cent among eighty-eight jejunal or gastrojejunal ulcers treated surgically at the Mayo Clinic prior to 1924. In a later report from the same clinic Walters and Clagett[3] found a gastrojejunocolic fistula to be present in twenty-three instances, or 13.6 per cent of 169 cases

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of gastrojejunal ulcer in which operation was performed during the years 1933 to 1936 inclusive.

Since the experience of any one surgeon in this field is not large, and since the number of cases seen in any one surgical clinic is relatively small, a survey has been made of all of the cases of gastrojejunocolic fistula at the University Hospital since its opening in 1925. During this period from 1925 to 1944, eighteen unmistakable cases of gastrojejunocolic fistula due to ulcer have been encountered. The earlier cases in this group were presented in a preliminary report on this subject by Rife,[4] in 1938. Fourteeen of the eighteen diagnoses were verified by surgical operation. In two of the cases the diagnosis was established beyond any doubt by clinical and roentgenologic evidence. Operation was advised but these patients refused treatment. In one instance, even though a positive diagnosis was made, no operation was advised because of the poor condition of the patient and his advanced age of 72 years. In only one instance was the diagnosis not made during life, being subsequently disclosed at necropsy.

From a study of the cases reported in the literature, it is evident that gastrojejunocolic fistula almost invariably occurs as a complication of a marginal or jejunal ulcer at the site of a gastroenteric anastomosis for duodenal ulcer. The great majority of cases occurs in instances of posterior gastrojejunostomy and much more often following simple short circuit operations rather than in cases of gastrojejunostomy associated with partial gastric resection. In the eighteen cases under discussion, duodenal ulcer was the primary lesion in every instance. It is a well-accepted fact that marginal ulcer rarely occurs following gastroenterostomy for gastric ulcer and is almost unheard of following gastroenterostomy for carcinoma of the stomach. It is often stated that gastrojejunocolic fistula and gastrojejunal ulcer very rarely occur in women, the reason for this being the lower values for gastric acidity in women as compared with men. In a group of fifty-two cases of marginal ulcer reported by Judd,[5] in 1935, there was but one woman patient. Seventeen of the eighteen patients were men, there being only one woman in the series. While the exact cause of marginal or jejunal ulcer is not known, the prevailing view is that these lesions most often occur in patients whose gastric acidity remains high following operation. This is much more apt to be true in gastroenterostomy or duodenal exclusion operations as contrasted with subtotal gastrectomy. High gastric acidity is also more likely to be present in the younger patients, in patients whose ulcer history is of short duration, and in those who are subjected to operation in the absence of proper indications or before a sufficient period of medical treatment has been tried.

The ages of the patients are given in Table I. Since gastrojejunal ulcer and gastrojejunocolic fistula are, in fact, artificial lesions, the age of the pa-

TABLE I. AGE INCIDENCE

AGE (YEARS)	NO. OF CASES
30 to 39 inclusive	5
40 to 49 inclusive	3
50 to 59 inclusive	7
60 to 69 inclusive	1
70 to 79 inclusive	2

Oldest patient, 72 years.
Youngest patient, 31 years.
Average age, 49 years, 5 months.

TABLE II. AGE AT TIME OF ORIGINAL OPERATION FOR ULCER

AGE (YEARS)	NO. OF CASES
20 to 29 inclusive	4
30 to 39 inclusive	6
40 to 49 inclusive	3
50 to 59 inclusive	4
Unknown years	1

Oldest patient, 58 years.
Youngest patient, 21 years.
Average age, 38 years, 6 months.

tient with this malady is roughly parallel to that of the patient at the time when the primary lesion, that is, duodenal ulcer, was treated by operation. It will be noted that the oldest patient in this series was 72 (two cases) and the youngest patient 31 years, the average age being 49 years and 5 months. The ages of these patients at the time of the original operation for ulcer are given in Table II. Here the oldest patient was 58 and the youngest 21 years, the average age at the time of the original operation being 38 years and 6 months.

The original operations performed for the primary duodenal ulcer are listed in Table III. Of interest is the fact that in all save one, the primary operation to be followed later by a marginal ulcer was a posterior gastroenterostomy. In the remaining case, a posterior gastroenterostomy was originally performed but due to a malfunctioning stoma, a secondary operation was necessitated during the same hospital stay and this corrective procedure consisted of a conservative gastric resection. According to the history in one case, two years following the gastroenterostomy a gastrojejunocolic fistula developed and was repaired elsewhere by a secondary surgical operation the exact nature of which is unknown, and at the time of the operation for the gastrojejunocolic fistula, the only remaining evidence of an earlier surgical procedure was the posterior gastroenterostomy. In spite of experience at this hospital and the experience of others indicating a high incidence of marginal ulcer following duodenal exclusion operations, such as the Devine or the Finsterer procedures, no instances of gastrojejunocolic fistula following such exclusion operations have been observed. Four of the original posterior gastroenterostomies were done at the University Hospital. One of these was performed for an uncomplicated duodenal ulcer and two for duodenal ulcer with pyloric obstruction. The remaining case was thought at operation to be one of nonresectable carcinoma of the pylorus and a palliative gastroenterostomy was performed. This patient remained well and symptom free for six years following the operation, whereupon he developed pain in the lower abdomen associated with the vomiting of blood. A diagnosis of a bleeding marginal ulcer was made and in spite of the fact that diarrhea developed after hospital entry, the diagnosis of gastrojejunocolic fistula was not made and the condition was revealed only at the necropsy. In Table IV is summarized the time interval between the original operation for ulcer and the operation performed for gastrojejunocolic fistula. It shows a great varia-

TABLE III. ORIGINAL OPERATION FOR ULCER

OPERATION	NO. OF CASES
P. G. E.*	10
P. G. E. (University Hospital)	4
P. G. E. and cholecystectomy	1
P. G. E., resection (malfunctioning stoma)	1
P. G. E. and closure acute perforation	1
P. G. E. (Repair "fistula" 2 years later)	1

*P. G. E., posterior gastroenterostomy.

TABLE IV. INTERVAL SINCE ORIGINAL OPERATION FOR ULCER

TIME (YEARS)	NO. OF CASES
Less than 2	2
2 to 5	4
6 to 10	3
11 to 15	6
Over 15	2

Longest interval, 26 years. Unknown "years," 1.
Shortest interval, 1 year. Average, 9 years, 6 months.

tion inasmuch as the longest interval was twenty-six years, the shortest interval one year, the average being nine years and six months. The patient was not certain as to how long before his University Hospital entry it was that the original gastroenterostomy had been performed, but it apparently was a matter of many years. A survey of the literature shows a great variation in this time interval between the original operation and the development of gastrojejunal ulcer and gastrojejunocolic fistula. Bornstein and Weinshel[6] mentioned one case in which a gastrojejunocolic fistula developed twenty-one years following a gastroenterostomy for duodenal ulcer. Probably the longest interval between the original gastroenterostomy and the occurrence of fistula is that recorded by Langemeyer[7] whose patient developed a gastrojejunocolic fistula forty years after an anterior gastroenterostomy.

In Table V is outlined the duration of the illness at the time of admission in the eighteen cases. For the most part the admission illness was fairly brief in duration, although for the group the average was approximately one year.

TABLE V. DURATION OF ILLNESS AT THE TIME OF ADMISSION

TIME	NO. OF CASES
Less than 3 months	5
3 to 6 months	5
7 to 12 months	2
13 to 18 months	2
19 to 24 months	2
Over 2 years	2

Average, 1 year.

SYMPTOMS

The clinical diagnosis of gastrojejunocolic fistula is ordinarily not difficult and in our cases was made correctly in all except the one instance already mentioned. The existence of this condition frequently can be suspected from the history alone. The patient, usually a man, gives a history of more or less typical ulcer symptoms for a variable period of time. A diagnosis of duodenal ulcer having been made, an operation, usually a posterior gastroenterostomy, is ultimately performed. Partial or complete relief of the ulcer symptoms follows for a period usually of months, possibly of years. In an analysis of sixty-seven cases of jejunal or anastomotic ulcers occurring following gastroenterostomy in their own clinic, Allen and Welch[8] found that one-third originated within the first year, and two-thirds within the second year following the primary operation. The beginning of new trouble may be marked by recurrence of the ulcer symptoms due to the recurrent marginal or jejunal ulcer. These symptoms may last for some time before the onset of the typical symptoms of gastrojejunocolic fistula. In other instances, however, there is no clear history indicative of marginal ulcer but the first symptoms of recurrent trouble are those so characteristic of gastrojejunocolic fistula. From a study of the life history of the disease, it would be expected that prior to the onset of the fistula, symptoms of an anas-

tomotic ulcer would usually be present. This, however, was not true in the majority of the cases herein reported, as only six, or one-third, of the eighteen patients gave such a history. The remaining twelve patients in this series apparently were relatively symptom free until the onset of the symptoms of fistula. Of the patients who had marginal ulcer symptoms prior to the fistula, bleeding was one of the most prominent.

Diarrhea.—Diarrhea is probably the most prominent and distressing symptom of gastrojejunocolic fistula and the condition which is chiefly responsible for the weight loss and the debilitated state of these patients. In some cases diarrhea is practically the only complaint, but more commonly this symptom is associated with others, such as abdominal pain, nausea and vomiting, flatulence, and eructations of foul gas described by the patient as having a fecal odor. Not infrequently blood appears in the stools, particularly at the beginning of the symptoms, presumably at the time when the marginal ulcer actually perforates into lumen of the colon. Five of the eighteen patients reported having had bloody or tarry stools on occasions prior to entry. It is said that following perforation, the ulcer itself heals, although in two of the three patients in our series examined at necropsy, multiple ulcers were present in the stomach and jejunum. One of the necropsies was done upon a patient who had not been operated upon and the other was done postoperatively. With the beginning of the trouble, the diarrhea may occur in episodes with comparative freedom from this symptom for brief periods. In most cases at the time of hospital entry, it had become more severe and persistent. Diarrhea was a prominent symptom in all of the eighteen cases and was the chief complaint in thirteen. Pfeiffer and Kent[9] were of the opinion that the diarrhea is not necessarily due to the entrance of undigested food directly into the colon from the stomach and in many instances even though the diarrhea is severe and persistent, the passage of large quantities of recognizable undigested food is not the rule. In their detailed histories, only six of the patients described undigested food in the stools. As the result of roentgen studies, Pfeiffer and Kent suggested that the diarrhea is really due to the regurgitation of colonic contents into the jejunum. This fecal matter from the colon proves irritating to the jejunum and provokes exceedingly active peristalsis, which in turn accounts for the abdominal cramps and the diarrhea. They stated that in their roentgenologic studies, barium from the stomach entered the colon rather slowly, even when the fistulous opening was large. On the contrary, barium administered by rectum promptly entered the stomach and the jejunum through the fistulous opening.

Vomiting.—Vomiting is probably the second most important symptom of patients with gastrojejunocolic fistula. It is often described as fecal, but as a matter of fact, it is not the stercoraceous vomiting such as is encountered in small bowel obstruction. It undoubtedly plays a considerable role in the dehydration and emaciation of patients and may bring about serious disorders in the body chemistry, such as alkalosis. Nine of the patients in the series gave a history of vomiting as an important symptom and in four of these the vomitus was feculent in character. Four patients who did not give a history of vomiting gave a definite history of fetid eructations.

Weight Loss.—Weight loss is an almost constant finding in these patients and in many instances reaches an extreme degree. Some degree of weight loss was present in all of the eighteen cases, the greatest loss recorded being 60 pounds, whereas the average weight loss was 33.3 pounds. This marked degree of emaciation is one of the important reasons why these patients are such poor

operative risks and why they are susceptible to infection in the peritoneal cavity as the result of contamination by fecal matter at the time of operation. In view of the mechanical nature of the lesion, any great improvement in the state of nutrition prior to operation is difficult or impossible.

Pain.—Pain of some degree is usually present. In those patients who have symptoms of marginal ulcer prior to the onset of fistula symptoms, the pain is usually of the type ascribed to stomal ulcer. Thus, it is more severe and more intractable to medical treatment than the primary ulcer pain and is often situated to the left of, and slightly below, the umbilicus. In the patients with fisula, oftentimes the pain is not characteristic and may be of the type of any colonic lesion, namely, in the lower quadrants of the abdomen. In a certain number of patients, pain appears to be due in part to some degree of mechanical intestinal obstruction. Obstruction may occur in the colon at the site of the perforation, which in turn results in constriction of the transverse colon by scar at this level or it may be due to small bowel obstruction, the obstruction involving the afferent segment of the jejunum employed in the original anastomosis. In still other instances, small bowel obstruction may occur from adhesions of unrelated loops of small bowel to the large inflammatory mass at the site of the fistula.

EXAMINATION

Physical examination on the whole aids but little in arriving at the correct diagnosis. The most important features observed are the emaciation and dehydration and the evidence of multiple vitamin deficiencies. Often a ventral hernia is found at the site of the former operative scar. Palpable masses within the abdomen and areas of localized tenderness are usually absent. Again, there may be signs of incomplete intestinal obstruction. This may occur in episodes. Due to the common occurrence of hypoproteinemia, nutritional edema may be observed. This finding was noted in ten of the forty patients reported by Atwater, Butt, and Priestley.[10]

LABORATORY EXAMINATION

Blood.—Anemia of moderate or severe degree is manifested by these patients. Two factors may be responsible. Deficiency of iron in the body due to failure of absorption will account for a hypochromic form of anemia. A deficit in the erythrocyte maturation factor of Castle in the intestine produces a macrocytic type of anemia. Fifty-two per cent of the forty cases studied by Atwater, Butt, and Priestley showed hemoglobin values below the normal range, and blood smears showed macrocytosis in 14 per cent.

Serum Proteins.—Serum protein determinations were made in ten of the cases. In all but one the values for total proteins were below normal. The lowest reading was 5.5 Gm. per cent and the average for this small group of cases was 6.16 Gm. per cent. Atwater, Butt, and Priestley found lowered values for serum proteins in 88 per cent of their patients tested, the lowest value being 3.7 Gm. and the average 4.9 Gm. per cent.

Blood Ascorbic Acid.—Determinations of the concentration of ascorbic acid in the blood were made in a small number of patients. All showed readings considerably below normal, the average reading for this group being 0.30 mg. per cent.

Prothrombin Clotting Time.—Due to the anatomic features involved in gastrojejunocolic fistula, there is likely to be impaired absorption of vitamin K from the intestinal tract with a resultant hypoprothrombinemia. Because of the

serious consequences at operation, if such a state is not recognized and corrected, the prothrombin clotting time should always be determined prior to operation. Atwater, Butt, and Priestley found a definitely prolonged time in 43 per cent of their cases studied in this manner.

ROENTGENOLOGIC EXAMINATION

Roentgen studies undoubtedly afford the most important means of proving the existence of gastrojejunocolic fistula. The diagnosis is often suggested or made following the administration by mouth of the barium meal when at the fluoroscopic examination barium is seen to enter the colon promptly (Fig. 1). However, when the fistula is small or if the barium enters the colon slowly this finding may be overlooked. As a part of the examination, the barium enema is

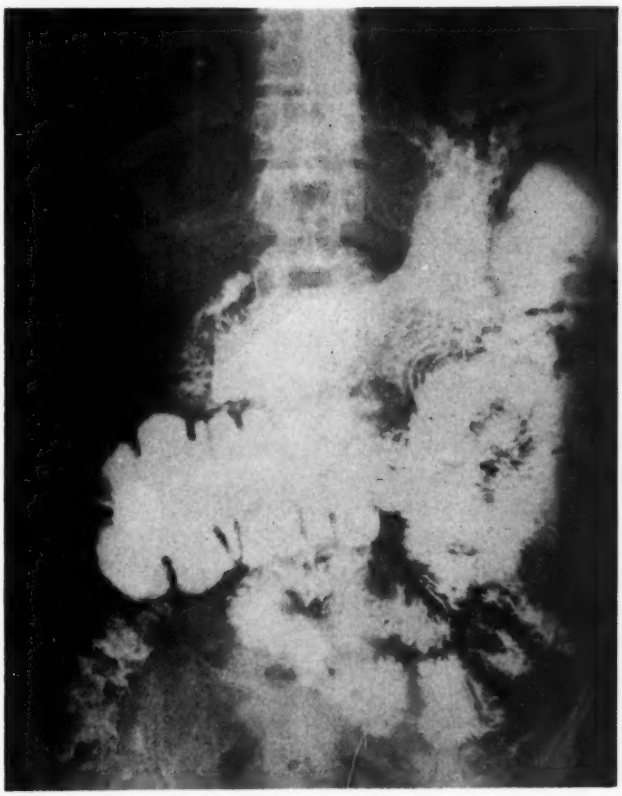

Fig. 1.—Roentgenogram taken shortly after the ingestion of barium and showing extensive filling of stomach, small bowel, and a portion of the transverse colon. On fluoroscopy the opaque fluid was seen to pass rapidly through a gastroenterostomy opening and resulted in immediate filling of the transverse colon. There was an exquisitely tender point over the stoma.

most helpful and important (Fig. 2). In the present series of cases, roentgenologic studies were carried out in every instance. In one case the examination was incomplete and unsatisfactory due to weakness of the patient and his inability to cooperate during the examination. Of the remaining seventeen cases the gastrojejunocolic fistula was demonstrated in fifteen, whereas in two the roentgen examination showed evidence of obstruction at the gastroenteric stoma. In both of these cases, however, the clinical data afforded convincing evidence of the presence of some type of internal intestinal fistula. Thus, by careful study the diagnosis rarely remains in doubt and with the diagnosis established, a regimen of suitable preoperative care may be instituted and the details of the operative procedure planned in advance.

TREATMENT

Preoperative Preparation.—Due to the cachectic state of these patients, ample time in the hospital before operation for the correction of the several nutritional disorders is essential. In the group of fourteen operative cases under discussion, the shortest period of preoperative preparation was two days, whereas the longest interval before operation was thirty-one days. The average for the group was 12.3 days. Due to the diarrhea and vomiting, there is usually dehydration, hence fluid balance must be restored and subsequently maintained. The vomiting causes chloride loss with a resultant alkalosis. Diarrhea, on the other hand, is apt to be responsible for abnormal sodium losses with

Fig. 2.—Roentgenogram taken following the introduction of barium per rectum. This shows extensive filling of colon, small bowel, and stomach. At the fluoroscopic examination marked spasm was noted in the mid-transverse colon. Small bowel filling occurred at this point and the cecum could not be well demonstrated.

acidosis as a consequence. Because of vomiting and rapid weight loss, ketosis is often present. Vitamin deficiencies are usually multiple and vitamin supplements are indicated. Blood transfusions are important in correcting secondary anemia and hypoproteinemia. None of the fourteen patients was treated by any form of chemotherapy before operation. With sulfasuxidine now available, its use before operation would seem to offer additional protection.

Operation.—The treatment of gastrojejunocolic fistula recommended by most surgeons in the earlier days consisted of disconnection of the three structures involved with closure of each and restoration to normal. Sometimes a pyloroplasty was added. The mortality was high due to the poor nutritional state of these patients and the more or less inevitable soiling of the peritoneum with fecal matter at the time of the operation. In order to solve this problem, a number of special procedures has been devised. Allen[11] has employed success-

fully a method of aseptic closure of the stomach and jejunum with aseptic resection of the involved segment of colon. This undoubtedly is of value in some of the smaller fistulas but does not seem to lend itself well to the larger and more complicated ones. Findlay[12] has advised a multistage operation utilizing the Mikulicz principle. The involved loop of transverse colon with the jejunal stump attached is exteriorized and subsequently removed. Scrimger[13] and Estes[14] have suggested gastric resection with exclusion of the fistula, which may be done with exenteration of the mucosa of the cuff of remaining stomach attached to the intestine. Of the more recent suggestions proposed, two of the most outstanding are those of Lahey and Marshall[15] and of Pfeiffer and Kent. The former propose a planned two-stage procedure. At the first stage the terminal ileum is transected, the distal end closed and dropped back into the abdominal cavity. The distal end of the proximal segment is then anastomosed side-to-side to the upper descending colon. By this procedure the intestinal stream is rerouted around the colic fistula, thereby excluding the involved segment of colon from the digestive tract and thus reducing to a minimum the contamination from the lower reaches of the intestine. The functional activity of the bowel is restored before the second stage, which is carried out about three months later. At this session, a block resection of the terminal ileum, right colon, transverse colon, and distal two-thirds of the stomach is performed. This procedure has been used in eight cases with one death. More recently Lahey[16] has reported one case in which, following the first stage procedure, the fistula healed spontaneously. While in his experience other fistulas have not closed spontaneously, he suggested that possibly a longer interval between stages should be allowed and that perhaps by so doing certain other fistulas might close spontaneously, thereby avoiding the necessity of a second stage.

Another suggestion in recent years and one that has received enthusiastic endorsement by many leading surgeons is the plan proposed by Pfeiffer and Kent in 1939. As the result of roentgenologic fluoroscopic examinations, they observed that the passage of material from the stomach into the colon is slow and the amount small. On the contrary, the regurgitation of colonic contents into the stomach and jejunum is rapid and provokes violent peristalsis due to the irritating effect of fecal matter in the jejunum and this in turn accounts for the diarrhea. Pfeiffer and Kent, therefore, performed a complete ascending colostomy as a first stage procedure. A remarkable improvement following this operation is reported. The patients gain in weight and in general health, and the second stage can be performed several months later. At this time a marked subsidence in the inflammatory reaction at the site of the fistula has taken place. In some of their cases, the second stage consisted of restoration to normal and in others of disconnection with gastric resection.

Operation.—In Table VI are given the various operative procedures employed in the fourteen patients treated surgically. In all of these cases the treatment has consisted of a one-stage direct attack. Obviously, no single procedure can be used in all cases as evinced by this list.

Recurrent gastrojejunal ulceration following gastrojejunostomy may occur as a true stomal ulcer situated directly at the anastomosis or as a jejunal ulcer located a variable distance from the anastomosis but practically always distal to it. Similarly, when fistula formation takes place, it may exist in either of these two forms. In only one of the fifteen cases in which the fistula was examined at operation or necropsy was there a true jejunocolic fistula. In this case the fistula was found 18 cm. distal to the gastroenterostomy. Here the

TABLE VI. OPERATIONS PERFORMED FOR REPAIR OF FISTULA

OPERATION	NO. OF CASES
Gastric resection Resection jejunum Closure colon	2
Gastric resection Closure jejunum Closure colon	2
Restoration, triple closure	5
Restoration, triple closure Pyloroplasty	2
Disconnection Resection jejunum Closure stomach Closure colon	1
(Postoperative polya) Disconnection Closure colon Reanastomosis stomach to jejunum Jejunojejunostomy	1
Separation jejunocolic fistula Closure jejunum Closure colon (Gastroenterostomy left intact)	1

surgical problem was relatively simple. The gastroenterostomy was left intact and a separation of the jejunum from the colon with closure of each of these structures was carried out. Ten of the remaining fourteen cases exemplified true gastrojejunocolic fistula while the remaining four evidently represented a complication of a jejunal ulcer which had developed only a few centimeters distal to the anastomosis. Because of the proximity of these latter jejunocolic fistulas to the gastroenterostomy, the surgical problem of repair was essentially the same as in the former group.

The size of the fistulous opening may vary considerably. In the fifteen cases, notes regarding the size are available in twelve. The largest opening was 6 cm. in diameter and the smallest 0.5 cm., the average being approximately 4 cm.

While gastric resection is undoubtedly desirable in preventing reactivation of the ulcer at a later date, it was performed in only four of the cases, the simpler procedures of restoration or restoration with pyloroplasty being adopted for the remainder of the group.

In the fourteen surgical cases, there were two operative deaths or a mortality of 14.3 per cent (Table VII). These fatal cases were the first and fourth in the series when the cases are arranged in chronologic order. The last ten consecutive operations have been performed without a fatality. One of the two fatalities involved a gastric resection, whereas the second consisted of a restoration with pyloroplasty only. The first patient died on the tenth postoperative day of peritonitis due to leakage at the suture line in the closed colon. The second death occurred on the eighteenth postoperative day, the patient having done well until that time. He suddenly went into shock and died shortly afterward.

TABLE VII. GASTROJEJUNOCOLIC FISTULA (14 OPERATIONS), OPERATIVE DEATHS (2), AND MORTALITY (14.3 PER CENT)

	OPERATION	NECROPSY
(1) 10th day	Gastric resection, resection jejunum, closure colon	General peritonitis Leakage of suture line in colon
(2) 18th day	Disconnection, closure stomach, Closure jejunum, closure colon, Finney pyloroplasty	Lung abscess, right lower lobe, with perforation into pleural cavity; all suture lines intact

Necropsy showed that death was due to the rupture of a lung abscess into the pleural cavity. Necropsy examination was done in both of these fatal cases. While every effort should be made to avoid contamination of the field at the time of operation, this is not always possible. Aseptic closures or anastomoses should be used if feasible. It should be remembered that the peritoneum has a strong defensive power against infection, although it undoubtedly is lessened in these debilitated patients. Peritonitis usually occurs from continued contamination from a leaking suture line or anastomosis, rather than from a single contamination. In this series of cases, intraperitoneal sulfonamide therapy was not employed. The status of the sulfonamide drugs intraperitoneally is not yet fully evaluated. In general this type of therapy has been used far less, with added experience in other related conditions, such as the surgery of the colon for carcinoma or chronic ulcerative colitis. In such cases unless there is gross contamination with extensive soiling of the peritoneal surfaces, intraperitoneal sulfanilamide or sulfathiazole is not now employed. As far as the abdominal wound is concerned, the most vulnerable tissue to infection is the subcutaneous fat, and wound infection in such cases is not infrequent. Wound sepsis occurred in six of the cases but fortunately was not severe in any. It is now believed that in all of these cases the method of delayed primary closure of the wound as proposed by Coller and Valk[17] should be employed.

END RESULTS

The end results in the fourteen cases are summarized in Table VIII. It will be noted that all three of the patients who survived an operation including gastric resection have remained well and free of ulcer symptoms. Of the nine

TABLE VIII. FOLLOW-UP STUDIES IN TWELVE CASES

RESULTS IN NINE OPERATIONS NOT INVOLVING GASTRIC RESECTION (FOLLOWED 3 TO 10 YEARS)	NO. OF CASES
End results	
Good	4
Recurrence of ulcer symptoms (Reoperation, 3)	5
RESULTS IN THREE OPERATIONS INVOLVING GASTRIC RESECTION	
End results	
Good	3

patients surviving the more conservative procedures, only four were well and symptom free. Five patients in this group developed definite recurrence of their old ulcer symptoms. Three of these patients subsequently returned to the hospital for further operative treatment (Table IX). The first case was one in which a conservative Polya resection had been done secondary to a gastroenterostomy complicated by a malfunctioning stoma. Recurrence of symptoms

TABLE IX. CASES REQUIRING SUBSEQUENT SURGICAL TREATMENT FOR ULCER

(1)	4/10/34 (Postoperative polya) Disconnection Closure colon Reanastomosis stomach to jejunum	7/20/34 Excision marginal ulcer Resection jejunum reanastomosis Jejunojejunostomy
(2)	1/11/37 Restoration	3/18/38 Devine exclusion operation for reactivated duodenal ulcer
(3)	2/10/39 Restoration	3/18/41 Gastric resection for reactivated duodenal ulcer (Hofmeister)

occurred a short time following discharge from the hospital and three months after the original operation for fistula, a secondary operation was performed. At this time the new marginal ulcer was excised and a restoration of the Polya anastomosis made. The jejunum at the site of the marginal ulcer was resected and an end-to-end anastomosis performed. Inasmuch as there tended to be some angulation of the jejunum due to adhesions, an additional jejunojejunostomy was performed. The second patient, approximately one year after a restoration operation, required further surgical therapy because of recurrence of the original ulcer symptoms. The original duodenal ulcer became reactivated and progressed to a stage of obstruction; accordingly, reoperation was necessary. Because of dense adhesions at the site of the original ulcer, a Devine exclusion operation was performed. The third patient, approximately two years after a restoration operation for fistula, developed recurrent symptoms from the original ulcer. These were sufficiently severe to demand further surgical therapy. At this secondary operation, the conventional type of subtotal gastrectomy according to the Hofmeister technique was carried out.

It is apparent that the best operation for the correction of gastrojejunocolic fistula is one in which subtotal gastrectomy is performed. However, with the possible exception of the stage operations of Lahey and Pfeiffer and Kent this often is not feasible or safe. Since simple restoration to normal has afforded complete relief in four of nine patients, this method has a definite place in the treatment of certain of these fistulas. This is particularly true inasmuch as many of these patients had meager indications for the original operation as compared with present-day standards. Moreover, should recurrence of the original ulcer take place, the more desirable operation may be performed with a patient in sufficiently good physical condition to withstand it. This is evidenced by that fact that there were no deaths among the three patients upon whom radical operations were subsequently performed.

OTHER GASTROENTERIC FISTULAS PRESENTING SIMILAR PROBLEMS

During the period of time covered in this report, certain other gastrocolonic fistulas due to primary disease were encountered (Table X). Four of these cases presenting somewhat similar problems were instances of primary carcinoma of the stomach in which spontaneous perforation into the transverse colon had taken place. In three cases exploration was carried out but the lesion was found to be hopelessly inoperable. In the remaining case of gastric carcinoma with gastrocolic fistula, a block resection of the involved segment of colon and lower portion of the stomach was successfully carried out. At the latest report, over two years later, this patient was free of recurrence. There was one case of carcinoma of the transverse colon with perforation into the stomach and a resultant gastrocolic fistula. Here no operation was advised. A single example was found of gastrocolic fistula secondary to tuberculous enteritis. This patient had pulmonary and intestinal tuberculosis and upon roentgen examination was found to have a gastrocolic fistula involving the stomach and the upper descending colon. Surgical treatment was not advised.

TABLE X. GASTROCOLIC FISTULAS DUE TO PRIMARY DISEASE

LESION	NO. OF CASES
Tuberculosis (pulmonary—intestinal)	1 No operation
Carcinoma of transverse colon	1 No operation
Carcinoma of stomach	3 Exploration only
Carcinoma of stomach	1 Block resection, recovery

A small but interesting group of cases is the one of gastroenteric fistula due to surgical errors. Four such cases have been encountered (Table XI). The first of these was one of gastrocolostomy, the original surgical operation having been performed five and one-half years previously for a duodenal ulcer with pyloric obstruction. Before leaving the hospital the patient complained

TABLE XI. GASTROENTERIC FISTULAS DUE TO SURGICAL ERRORS

Gastrocolostomy Duodenal ulcer, obstruction Operation, 5½ years previously Vomiting, diarrhea since	Disestablishment, cure
Gastroileostomy Duodenal ulcer, acute perforation Operation, 3 years previously Diarrhea since	Disestablishment, cure
Gastroileostomy Duodenal obstruction Operation, 7½ years previously Diarrhea since	Disestablishment, cure
Gastroileostomy "Ulcers" Operation, 15 years previously Obstructive symptoms	Disestablishment, gastric resection (Finsterer), death

of fecal vomiting and ever since the operation had continued to have both vomiting and diarrhea. At the time of the second operation, an anastomosis was found to have been made between the greater curvature of the stomach and the distal transverse colon. The treatment consisted of disestablishment of the anastomosis and the patient promptly improved, subsequently remaining well. Three examples of gastroileostomy were encountered. All of the original operations had been performed for duodenal ulcer. Two of these patients had had diarrhea dating from the time of the original operation. The other patient had had a gastroenterostomy fifteen years before and for a number of years following it had symptoms of partial or incomplete small bowel obstruction. Diarrhea was not an important symptom in this case. In two of these cases of gastroileostomy the treatment consisted of disestablishment with prompt recovery. In the remaining case, the anastomosis was disconnected and a gastric resection by the Finsterer method was performed. Death occurred on the ninth day, from peritonitis. Necropsy disclosed that this was due to leakage of the closed distal antral end of the stomach.

SUMMARY

1. Forty-seven patients with marginal or jejunal ulcer were treated surgically at the University Hospital during the period 1934 to 1944. Eight patients, or 17 per cent of the surgical cases, had the serious complication of gastrojejunocolic fistula.

2. During the period 1925 to 1944, eighteen unmistakable cases of gastrojejunocolic fistula have been observed. Fourteen of these patients were treated by surgical operation.

3. All of these cases of gastrojejunocolic fistula represented a late complication of posterior gastroenterostomy for duodenal ulcer.

4. The longest interval between the original operation for ulcer and the hospital entry for fistula was twenty-six years; the shortest interval was one year and the average time nine years and six months.

5. Nearly all patients exhibited serious nutritional disturbances requiring

intensive preoperative treatment. The time spent in the hospital prior to operation ranged from two to thirty-one days, the average time being 12.3 days.

6. The surgical operation in all cases consisted of a one-stage procedure. In ten instances a restorative type of operation was performed, whereas in four cases, gastric resection was included. There was one postoperative death in each group, or a mortality of 14.3 per cent for the entire series.

7. Follow-up studies showed that all patients who survived operations involving gastric resection had good results, whereas, only four of the nine patients surviving the more conservative operative procedures remained free of ulcer symptoms. Three of the five patients with recurrent ulcer subsequently required further surgical therapy. No deaths occurred among these patients who later required reoperation. While gastric resection is ordinarily desirable at the time of the operation for the repair of the fistulas, it is not always feasible or safe. Restoration of the tract to normal, therefore, is a useful procedure in certain cases. This is particularly true inasmuch as many of the original gastroenterostomies were performed upon meager indications as judged by present-day standards. If further surgery for recurrence of the ulcer later becomes necessary in certain cases, subtotal gastrectomy can be carried out upon a patient in good condition with a very low mortality.

8. Gastrocolic fistulas due to primary disease of the stomach or colon are discussed. These patients present similar problems in preoperative care and in certain matters of surgical technique.

9. A small group of gastroenteric fistulas due to surgical errors at the time of the original operation for ulcer is considered briefly.

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CARCINOMA OF SIGMOID AND RECTOSIGMOID INVOLVING URINARY BLADDER

Surgical Management in Sixty-Four Cases

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SOME carcinomas of the sigmoid and rectosigmoid give rise early in their course to widespread metastatic growths. Others, over a period of many months or even years, grow to large size, perforate the confines of the bowel, invade adjacent tissues and organs, and cause death without extension to more distant parts of the body.

At present, surgical therapy for carcinoma of the sigmoid and rectosigmoid with distant metastasis is amenable only to palliative treatment. However, the condition is seldom inoperable because of local extension of the disease. When the uterus, ovaries, or fallopian tubes are involved secondarily these organs, with the diseased portion of intestine, can be removed readily. If one ureter is involved, it can be excised provided the opposite kidney and ureter are functioning normally. Portions of the abdominal wall, spermatic or ovarian vessels, common iliac vein and segments of small intestine that are secondarily infiltrated with carcinoma can be extirpated with the primary growth. However, if the urinary bladder is involved the difficulties of resection are increased. It therefore seems advisable to point out some of the problems associated with carcinoma of the sigmoid and rectosigmoid involving the urinary bladder and to review our experiences with its surgical management. This study is based on sixty-four consecutive cases, in which operation was performed by the senior author in the years 1931 to 1943, inclusive.

DIAGNOSIS

It is often difficult or impossible to detect preoperatively early invasion of the urinary bladder by a malignant process located in the sigmoid or rectosigmoid. Slight involvement of this organ usually is not evident on clinical or laboratory examinations and most often is discovered on surgical exploration.

If extensive involvement of the urinary bladder is present, there may be distressing urinary symptoms to aid the clinician in establishing the diagnosis preoperatively. Pain and discomfort in the bladder, relieved by the passage of flatus or stool, is characteristic. Nocturia, frequency and urgency of urination may be present. If the malignant process invades the lumen of the bladder, a colovesical fistula may ensue. In such instances the passage of gas and feces by way of the urethra establishes the diagnosis of enterovesical fistula. In one of our cases gross hematuria was the only complaint. In the usual history, however, the symptoms referable to the bowel so completely overshadow those referable to the urinary tract that the latter are overlooked unless a careful report is obtained.

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In a few cases of extensive invasion of the urinary bladder it is impossible even by careful questioning to elicit a history of urinary symptoms. In these cases, however, the presence of pyuria may suggest to the clinician the possibility of secondary involvement of the urinary bladder. In twenty-one of the sixty-four cases on which this paper is based, in which the entire vesical wall was invaded by carcinoma, eleven (50 per cent) patients had a significant degree of pyuria preoperatively. Proctoscopic examination and roentgenologic investigation of the colon after a barium enema may reveal fixation of the intestinal lesion in the region of the urinary bladder and thus aid in establishing the diagnosis.

When secondary invasion of the urinary bladder is suspected preoperatively the patient should undergo thorough urologic investigation. Cystoscopic examination aids in determining the extent and situation of the malignant process. Carcinomas of the sigmoid or rectosigmoid that involve the urinary bladder usually involve the dome or posterior wall. In these cases the results of surgical measures have been satisfactory. When the malignant process extends downward, however, and cystoscopic examination reveals extensive invasion of the region of the trigone, the condition is one which is ordinarily not amenable to surgical therapy. Excretory urograms also provide valuable information if, during operation, one ureter must be excised in order to remove the growth.

PREOPERATIVE PREPARATION

The patient should be hospitalized preoperatively for a sufficient period of of time to permit proper evaluation of, and improvement in, his general condition. Urinary antiseptics may be administered. Appropriate procedures should be instituted concomitantly to prepare the bowel for surgical operation. Retained fecal material can be eliminated by the use of a saline laxative and enemas of warm tap water. The bulk of the stools can be reduced by a nonresidue type of diet. Coliform bacteria in the intestinal contents can be reduced in number, or eliminated, by the administration of large doses of succinylsulfathiazole for at least three days prior to operation.

SURGICAL TECHNIQUE

An incision of the splitting or retracting type, which provides optimal exposure, is made in the lower left rectus muscle. If abdominal exploration does not reveal hepatic or other distant metastatic growths, resection can be undertaken immediately.

Resection of the bladder is performed first (Fig. 1). This is begun by making an incision through the uninvolved portion of the wall of the bladder, adjacent to the lesion, high up on the dome and away from the trigone. The leakage of urine can be controlled almost completely by catheterization of the patient immediately preoperatively and by maintenance of constant suction in the pelvis during the operation. The involved portion of bladder is next resected, the incision being carried downward and completely around the affected portion. In this manner, one-half or more of the bladder can be removed. If the trigone is visualized soon after the bladder is opened there is little danger of injury to important structures located in that region.

The opening in the bladder thus produced is then allowed to remain. Constant suction is instituted to avoid any undue urinary spillage.

The involved portion of intestine is resected next, for these reasons: (1) The vesical portion of the fistulous tract now lies free in the pelvis and, if a colovesical fistula exists, serious fecal contamination is a possibility. (2) The

bladder usually is closed around a suprapubic cystostomy tube, which, if inserted before the intestinal segment is resected, is kept out of the operative field with difficulty. (3) Further mobilization of the peritoneum of the bladder may be necessary in order to reperitonealize the pelvic floor. If the bladder is closed prematurely the suture line may be disturbed by this maneuver.

The primary lesion is removed by resection of an uninvolved segment of intestine proximal to the tumor, a lesser amount distal to it, and a large wedge of the adjacent mesentery (Fig. 2). If the distal portion of the bowel remaining after such a resection does not extend above the brim of the true pelvis, the superior hemorrhoidal vessels always are included in the resection. The distal segment will receive an adequate blood supply from the middle and inferior hemorrhoidal arteries, and by removing the superior hemorrhoidal vessels a more thorough extirpation of adjacent lymph nodes can be obtained.

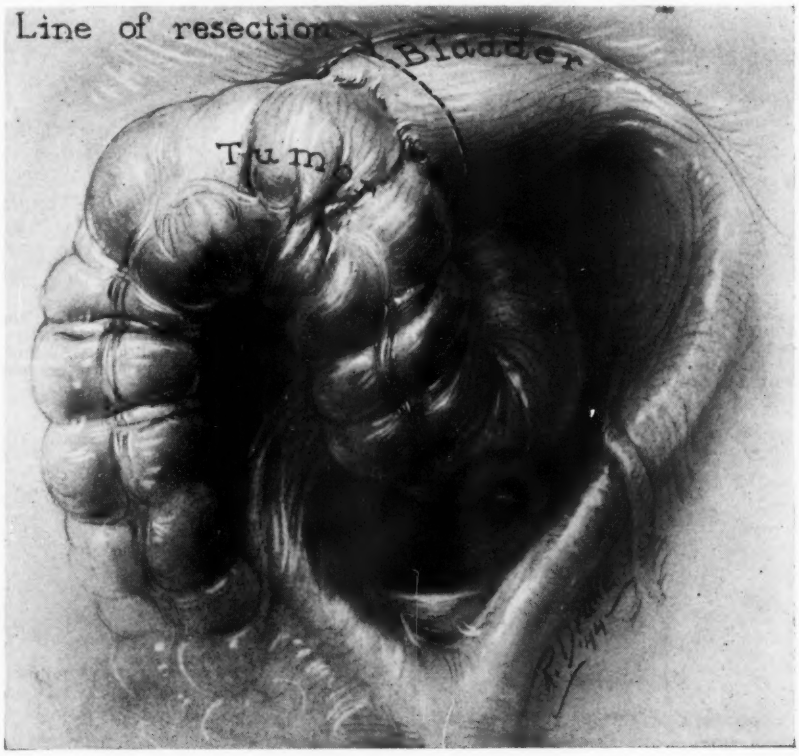

Fig. 1.—A large perforating carcinoma of the lower portion of the sigmoid is firmly adherent to the urinary bladder. Dotted line indicates proposed line of resection of bladder.

After resection is completed, a decision must be made concerning the disposition of the two remaining cut ends of intestine. If both segments are long enough to permit bringing them into apposition on the anterior abdominal wall, an exteriorization type of procedure can be employed (Case 1). In this operation the two ends of bowel emerge from the abdomen through the primary incision or through a stab incision and are held in position by a three-bladed clamp. If the distal segment of intestine is too short to reach to the abdominal wall but the two ends can be approximated (Case 2), the operation is completed as in the so-called "anterior resection" (Fig. 3, inset). Curved rubber-covered clamps are used and end-to-end colocolostomy is performed. A single row of interrupted catgut sutures usually suffices for the posterior part of the anastomosis. The anterior part of the anastomosis is completed with two rows of running catgut sutures. Whenever such an anastomosis is made low in the in-

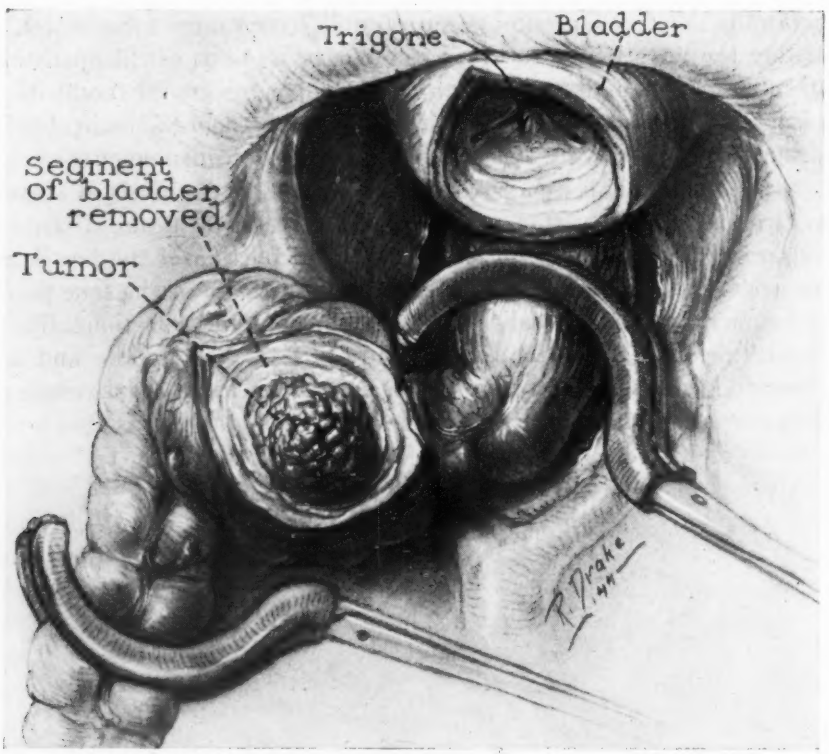

Fig. 2.—The involved portion of vesical wall, including a cuff of normal tissue, has been completely resected. The peritoneum has been incised medially and laterally and the rectosigmoid and upper part of the rectum have been freed from the hollow of the sacrum. The curved clamps indicate the points at which the bowel will be severed after resection of the adjacent mesentery and superior hemorrhoidal vessels.

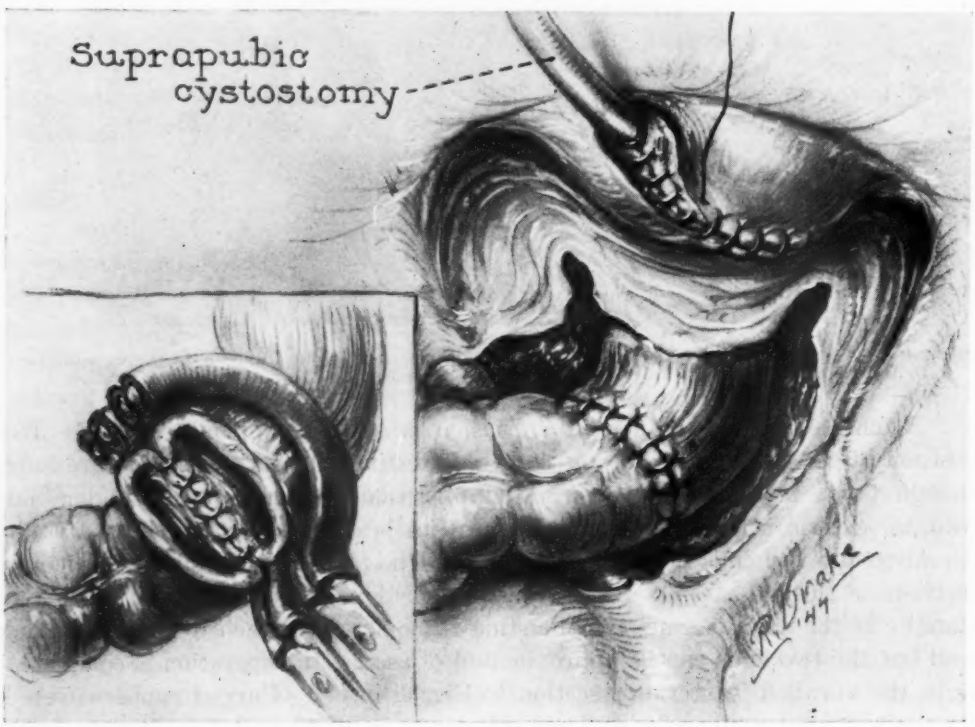

Fig. 3.—Over curved rubber-covered clamps an open type of end-to-end anastomosis is performed. Interrupted sutures which include all layers suffice for the posterior row (inset). The anastomosis then is completed. The urinary bladder is closed around a suprapubic cystostomy tube of large caliber. Following this the pelvic floor will be peritonized in such a manner as to place the colonic anastomosis in a retroperitoneal position.

testine this segment must be defunctionalized for two to three weeks by establishing a loop colostomy proximal to the anastomosis. A segment of transverse colon, brought out through a stab wound in an upper midline position, usually serves the purpose, and requires only a few minutes of operating time (Fig. 4).

Anastomoses low in the pelvic colon have a tendency to "leak." The distal segment is often the upper rectum or the rectosigmoid, which has been mobilized from the hollow of the sacrum and obviously does not have a serosal or peritoneal covering. Therefore, satisfactory anastomosis is dependent on the sutures in the mucosal and muscular layers of the intestinal wall. If a colostomy proximal to the lesion is performed, little or no difficulty is experienced, but if the content of the bowel passes over the site of anastomosis before healing has occurred, pelvic inflammation and inflammatory granulomas in this area sometimes result.

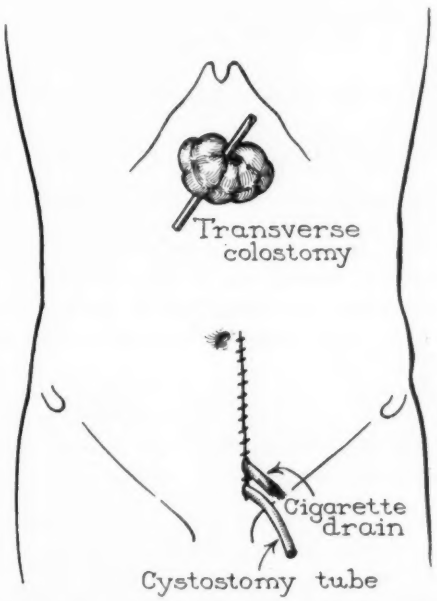

Fig. 4.—Temporary colostomy has been performed by bringing out a loop of transverse colon through an upper midline stab incision. The suprapubic cystostomy tube emerges from the lower angle of the operative incision. Immediately above it is a Penrose drain which extends down to the site of anastomosis in the hollow of the sacrum.

If, after resection, neither of the previously described procedures is applicable, both ends of the bowel can be inverted provided colostomy proximal to the lesion previously was performed (Case 3). If colostomy was not performed previously, a single-barrel colostomy can be provided, the proximal end of the bowel being brought out onto the anterior abdominal wall, and the distal stump can be inverted (Case 4).

After resection of the colon the opening in the bladder is closed snugly around a suprapubic cystostomy tube (Fig. 3). Two layers of running sutures of plain catgut, the first of which is essentially a mucosal layer and the other a serosal or muscular layer, are supplemented by a row of interrupted serosal sutures. When extensive resection of the bladder has been performed it is probably inadvisable to depend on a urethral catheter for drainage of the bladder. Because of the necessarily small caliber of such catheters, they may become plugged and urine may leak into the abdominal cavity through the suture line. This danger is minimized if a suprapubic cystostomy is performed and a 26 or 28 French catheter is inserted. The suprapubic cystostomy tube of large caliber is brought out through the most anterior portion of the bladder incision, through

the space of Retzius, and is sutured into the lower angle of the primary incision (Fig. 4). This tube is easily removed in two or three weeks and the resulting urinary fistula rapidly closes spontaneously.

Resection of the bladder also can be performed in the course of radical posterior resection by cautery (Case 5) or in the course of the combined abdominoperineal operation (Case 6). When the growth is so low in the rectosigmoid that one of these two types of operation is indicated, the involvement of the bladder often is near the trigone and especial care is necessary to avoid injury of vital structures in this region.

REPORTS OF CASES

CASE 1.—A white man, 70 years of age, was operated on for a huge tumor in the lower part of the sigmoid, which had infiltrated into a large portion of the urinary bladder. The sigmoid and a considerable portion of the urinary bladder were removed. Double-barrel colostomy was performed, the cut ends of the colon being exteriorized and held in position on the abdominal wall with a three-bladed clamp. The urinary bladder was closed around a suprapubic cystostomy tube.

The pathologists reported the lesion to be an adenocarcinoma, grade 3 (Broders) and type C.*

Later the colonic stoma was closed. The patient was alive and well five years later.

CASE 2.—A white woman, 47 years of age, had extensive carcinoma of the lower part of the sigmoid. The lesion also involved the uterus and urinary bladder. Preliminary colostomy had been performed elsewhere. The involved portion of bowel, adjacent mesentery, uterus, both fallopian tubes and ovaries, and a large portion of the urinary bladder were removed. Continuity of the bowel was established by end-to-end anastomosis of the middle portion of the sigmoid to the upper part of the rectum. The urinary bladder was closed around a suprapubic cystostomy tube.

The lesion was an adenocarcinoma, grade 2 (Broders) and type C (Dukes), which extended completely through the uterus and also involved the urinary bladder.

Subsequent to resection the colonic stoma was closed. The patient died two years after operation, of abdominal carcinomatosis.

CASE 3.—A white man, 42 years of age, had a large carcinoma of the rectosigmoid which practically filled the true pelvis and involved secondarily the posterior wall of the bladder and the terminal portion of the ileum. Preliminary colostomy was performed in the descending segment of colon. Later the involved portion of the colon, the terminal part of the ileum, and about two-thirds of the urinary bladder were resected. The cut ends of the rectum and sigmoid were inverted. Continuity of the small bowel was obtained by end-to-end anastomosis. The urinary bladder was closed around a suprapubic cystostomy tube.

The pathologist reported the lesion to be grade 2 (Broders) and type C (Dukes) colloid adenocarcinoma.

The patient died on the seventh postoperative day, of generalized peritonitis.

CASE 4.—A white man, 57 years of age, had a large, perforating carcinoma of the middle portion of the sigmoid, which secondarily had involved the terminal part of the ileum and the urinary bladder. The sigmoid, 17 cm. of ileum, and a large portion of the dome and posterior wall of the bladder were resected. Because resections of portions of the ascending colon and of the descending colon had been performed seventeen and seven years previously, respectively, the descending colon could not be mobilized sufficiently to allow its anastomosis with the rectosigmoid at this operation. Accordingly, the end of descending colon was brought out through a stab incision in the abdominal wall to provide a single-barrel colostomy and the rectosigmoid was inverted. Side-to-side ileo-ileostomy restored continuity of the small intestine. The bladder was closed around a suprapubic cystostomy tube.

The lesion proved to be a grade 1 (Broders) and type C (Dukes) colloid adenocarcinoma.

This patient was alive and well six months after operation.

CASE 5.—A white man, 65 years of age, had a large carcinoma of the rectosigmoid and rectum that also involved the urinary bladder and prostate gland. Preliminary sig-

*Dukes, C. E., Classification of Cancer of Rectum, J. Path. & Bact. 35: 323-332, 1932.

moidostomy (loop type) was performed. Three weeks later radical posterior resection of the rectum, rectosigmoid, and lower sigmoid was performed by cautery. The involved portions of the prostate gland and urinary bladder also were removed. The distal end of sigmoid was inverted and replaced in the peritoneal cavity. The opening in the urinary bladder was closed with interrupted sutures of catgut. Drainage of the bladder was provided by use of a urethral catheter.

The pathologists reported the lesion to be a colloid adenocarcinoma, grade 2 (Broders) and type C (Dukes).

This patient was alive and well five years later.

CASE 6.—A white man, 53 years of age, had a large obstructive type of carcinoma of the rectosigmoid which was firmly adherent to the base of the urinary bladder. A combined abdominoperineal resection was performed in two stages. A large portion of the posterior wall and base of the bladder, just above the trigone, was involved. This segment of bladder was resected and the opening was closed through the anterior abdominal incision.

The pathologists reported the lesion to be an adenocarcinoma, grade 2 (Broders) and type C (Dukes).

The patient died on the twenty-second postoperative day from pulmonary embolism and pneumonia.

DISCUSSION

Of the sixty-four patients in the present series, fifty-nine were men and five were women. The apparent infrequency of involvement of the urinary bladder in this condition in women, in comparison with men, is evidently attributable to anatomic differences in the pelvis. In women the uterus, broad ligaments, ovaries, and fallopian tubes are interposed between the urinary bladder and the pelvic colon and thus protect the urinary bladder against invasion by carcinoma originating in this portion of the intestine. In four of the five women in this series the uterus and its appendages also were extensively infiltrated by the disease. In such instances cure is possible only if the involved portions of the uterus and its appendages are removed together with the affected portions of the bladder and colon. The ages of the sixty-four patients varied from 29 to 76 years, the average age being 55 years.

Involvement of the urinary bladder usually does not occur in the early stages of malignant processes of the pelvic colon. It is most commonly a late phenomenon which eventuates only after the tumor has attained a large size and has extended beyond the confines of the intestine. In the majority of cases carcinoma has been present for a long time and it is therefore not surprising that many patients are in poor general condition.

Probably the first step in invasion of the urinary bladder by carcinoma of the sigmoid or rectosigmoid is an inflammatory attachment of the tumor to the peritoneal covering of the bladder. This situation sometimes is encountered at operation. In such a case the malignant process can be dissected from the urinary bladder without making an opening into its lumen. The examination of small bits of tissue from the vesical wall at the site of attachment will reveal the presence or absence of residual carcinoma and will allay any doubt in the surgeon's mind as to whether the malignant process has been completely eradicated. The inflammatory reaction around a secondary malignant growth of the bladder is not only a phenomenon of the early stages but also of the later stages of the malignant disease. Often advanced carcinoma that has extensively infiltrated the wall of the bladder is surrounded by such a severe inflammatory reaction that it is difficult to determine, even at operation when the lesion is in full view and can be examined by the palpating hand, whether the reaction is primarily inflammatory or neoplastic.

When a large carcinoma in the sigmoid or rectosigmoid has extended to the urinary bladder and is surrounded by an indurated inflammatory reaction,

the surgeon may be tempted to perform colostomy and to wait several weeks for the inflammation to subside before undertaking resection of the bowel. Undoubtedly this is often a valuable procedure but the senior author recently has concluded that postponement of resection after the distal segment of colon has been defunctionalized usually will not appreciably diminish the inflammatory reaction if the malignant growth has penetrated completely through the wall of the bladder. In such instances the urine and the diseased condition of the bladder continue to "feed" the infection in spite of the use of urinary antiseptics. Therefore, it has become the senior author's practice to resect such lesions primarily whenever the general condition of the patient warrants the procedure.

In forty-two of the sixty-four cases in this series the condition was classified as operable. Two patients in the group who had presumably removable lesions died after colostomy. In the remaining forty cases, resections were performed. In nineteen of the forty cases the attachment to the bladder was of an inflammatory nature and removal of the tumor did not necessitate an opening into the lumen of the bladder. In the remaining twenty-one cases, portions of the full thickness of the vesical wall were removed. In fifteen of these, approximately one-third or more of the organ was resected; in six cases smaller segments were resected.

In most of the cases resection of the bowel was completed by end-to-end anastomosis. Anterior resection with end-to-end colocolostomy was performed on sixteen of the forty patients who underwent resection. In ten cases the segments of bowel were of sufficient length following resection to permit the ends to be exteriorized. In three cases, loop colostomy proximal to the anastomosis was performed and after resection both ends of the colon were inverted. In four cases the cut end of the distal segment of intestine was inverted, and the proximal end was used in performing single-barrel colostomy. Resection of the bladder was carried out in three cases at the time of combined abdominoperineal resection, and in four cases in conjunction with radical posterior resection by cautery.

Only palliative operations could be performed in twenty-two of the sixty-four cases. In eight of these twenty-two cases, metastatic growths in the liver, lungs, or other distant organs were present. In seven cases the carcinoma was irremovable because it was extremely large and had infiltrated extensively into the bladder and other pelvic organs. In seven cases the patient was debilitated, anemic, cachectic, and in such poor general condition that resection was considered inadvisable. Roentgen or radium therapy often was employed when removal of the carcinoma was contraindicated because of the poor general condition of the patient.

SURVIVAL RATES

Of the forty patients subjected to radical resection, twenty were still living at the time of inquiry between March and September, 1944, or had survived for five years or longer, as shown in Table I. Of these, seven have lived for more than five years since operation, two for four years, one for three years, two for two years, and five for one year. In three cases the operation was performed less than one year prior to preparation of this report in October, 1944.

The cases in this series in which cures have existed for the longest periods are not limited to those in which early or slight involvement of the urinary bladder was present. Of the ten patients who have survived for three years or longer, seven were classified as having a slight to moderate degree of bladder

infiltration; three had massive involvements necessitating extensive resection of the urinary viscus.

Thirteen patients died after leaving the hospital. The shortest duration of life was two months. Several patients survived for more than two years, however.

Resection of the urinary bladder in the course of radical operations for the cure of carcinoma of the sigmoid or rectosigmoid entails an increased operative risk. Seven of the forty patients who underwent radical resection died in the hospital. Bronchopneumonia was responsible for death in two cases, pulmonary embolus in two, peritonitis in one, liver abscess in one, and intra-abdominal hemorrhage in one.

TABLE I. SURVIVAL AFTER RESECTION IN CASES OF CARCINOMA OF SIGMOID AND RECTOSIGMOID

YEARS	CASES
5 or more	7*
4	2†
3	1†
2	2†
1	5†
Less than 1	3†

*Recent follow-up not attempted in cases in which patients were known to have survived for five years.

†Inquiry made between March and September, 1944.

SUMMARY AND CONCLUSIONS

1. Carcinoma of the sigmoid and rectosigmoid may invade the urinary bladder and other adjacent structures without producing distant metastatic growths. Such lesions are often amenable to resection through the abdominal wall. If this is not feasible, the combined abdominoperineal operation or radical posterior resection can be considered.

2. A small amount of secondary invasion of the urinary bladder by carcinoma of the sigmoid or rectosigmoid may give rise to no clinical or laboratory findings. More extensive involvement often produces distressing urinary symptoms and pyuria.

3. Of sixty-four patients who had carcinoma of the sigmoid or rectosigmoid involving the urinary bladder, forty patients underwent extensive resection. There were seven operative deaths. Twenty of the forty patients are still living, having survived for from less than one to more than five years after operation. Seven have lived for five years or longer.

SUCCINYLSULFATHIAZOLE AND INTESTINAL SUCTION IN SURGERY OF THE LARGE BOWEL

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THERE have been two recent important improvements in the preoperative preparation of patients for large bowel surgery. The first is the use of the Miller-Abbott tube and the second is the use of chemotherapy to minimize the number and virulence of organisms within the lumen of the bowel. This paper is a statistical report of our experience at the Peter Bent Brigham Hospital with these two adjuncts to surgery of the colon. It compares the results in a series of consecutive cases of large bowel resections prepared by these two techniques with a comparable series in which these techniques were not used.

Until recently, proximal colostomy has been widely used in preparing patients for resection of the large bowel. The advantage of preliminary colostomy is that, preoperatively, the bowel is relieved of distention and may regain its function and the distal lumen may be nearly emptied of its contents; postoperatively, the site of anastomosis is kept at rest and the risk of "blowout" at the suture line from increased intraluminal pressure due to temporary obstruction at the anastomosis is minimized.

When the Miller-Abbott tube was introduced,[1] which could apply intraluminal suction drainage to the lower ileum or right colon, Whipple used it to obviate the necessity of preliminary colostomy.[2] His results were so good that Miller-Abbott tube drainage of the lower ileum was adopted as a routine measure in the preparation for elective large bowel surgery at this clinic and supplanted the routine proximal colostomy.

A special risk of surgery upon the large bowel is infection. Sterilization of the lumen would be the ideal plan for preoperative preparation. Poth and Knotts and associates[3, 4] introduced succinylsulfathiazole as an agent to reduce greatly the number of large bowel bacteria. They have reported good results when it is used in preparation for large bowel surgery.[5, 6] Other reports of its successful use have been made by Firor,[7] Archer and Lehman,[8] and Behrend.[9]

SELECTION OF CASES

The control group of cases in this study includes patients who had resections of the large bowel between 1938 and 1942. This interval was selected because all the operations are recent enough to be well within the period of modern parenteral therapy and postoperative care. Preliminary colostomy was the routine procedure in this group of cases when the patients were to have primary anastomosis. The test group of cases includes those in which the patients were operated upon since 1942. It differs from the control group only in that all patients were prepared by introduction of the Miller-Abbott tube and the administration of succinylsulfathiazole.

PREOPERATIVE CARE

The patients in the control group were prepared for operation by saline catharsis, enemas, low residue, high vitamin, high caloric diet, and proximal colostomy was performed if a primary anastomosis was contemplated.

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Mineral oil by mouth for one day only was given in the test cases. The sulfasuxidine* was then administered after the technique of Poth[6]; 0.5 Gm. per kilogram of body weight was given during the first day, and thereafter 0.25 Gm. per kilogram of body weight during each succeeding day. The drug was given in six equal doses per day and continued for four to twelve days, usually five or six days before operation. The patients were carefully observed for evidences of toxic reactions to sulfathiazole,[10] although none appeared.

Two days before operation the Miller-Abbott tube was introduced. In general the tip passed the pylorus with little difficulty.† Suction was maintained during the passage of the tube. The day before operation, the position of the tube was checked by x-ray. Operation was not undertaken until the end of the tube was in the lower ileum (Fig. 1). During the preoperative period, high vitamin, high caloric, low residue diet was given. Feeding was interrupted only while the tip of the tube was in the stomach.

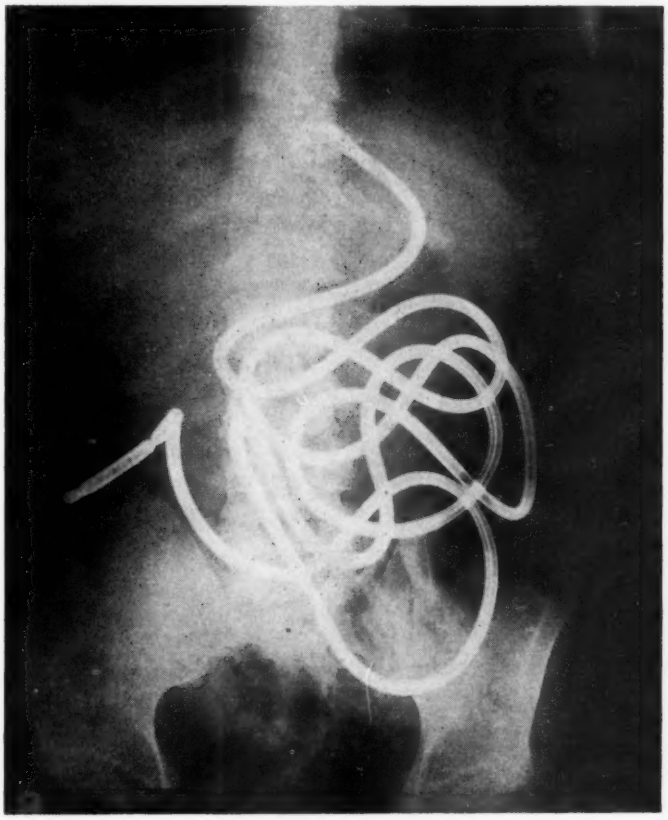

Fig. 1.—X-ray check shows the tip of the Miller-Abbott tube in the lower ileum, the ideal preoperative position.

During operation, the tube was kept in place. Suction was maintained in the postoperative period until good peristalsis could be heard. Suction was then temporarily discontinued and if distention did not appear and the patient passed flatus and feces, the tube was removed. Usually the tube was left in place until the fifth or sixth postoperative day. If there was doubt whether the tube should be removed, it was left in place for a day or so more.

*N^4 succinylsulfathiazole is registered under the proprietary name of sulfasuxidine by Sharp and Dohme, Inc., Philadelphia, Pa.

†A technique which seems to have assisted in passing the tip of the tube through the pylorus consists in tying one end of about eighteen inches of plain catgut to the bucket tip of the Miller-Abbott tube. When the tip of the tube is in the stomach, the free end of the catgut passes easily through the pylorus and directs the tip of the tube into the pylorus. The catgut is soon digested in the small bowel and disappears.

OPERATIVE PROCEDURES

The type of resection and anastomosis in the test group was the so-called "closed" type except when ileotransversecolostomy was performed after right colectomy; then the procedure was "open." The technique of resection and end-to-end anastomosis used is illustrated (Fig. 2). It was carried out with fine silk sutures, using two or occasionally one row of interrupted Halsted sutures.

RESULTS

Comparison of all cases of each group shows that when the Miller-Abbott tube and sulfasuxidine were used, there was a reduction in the mortality from

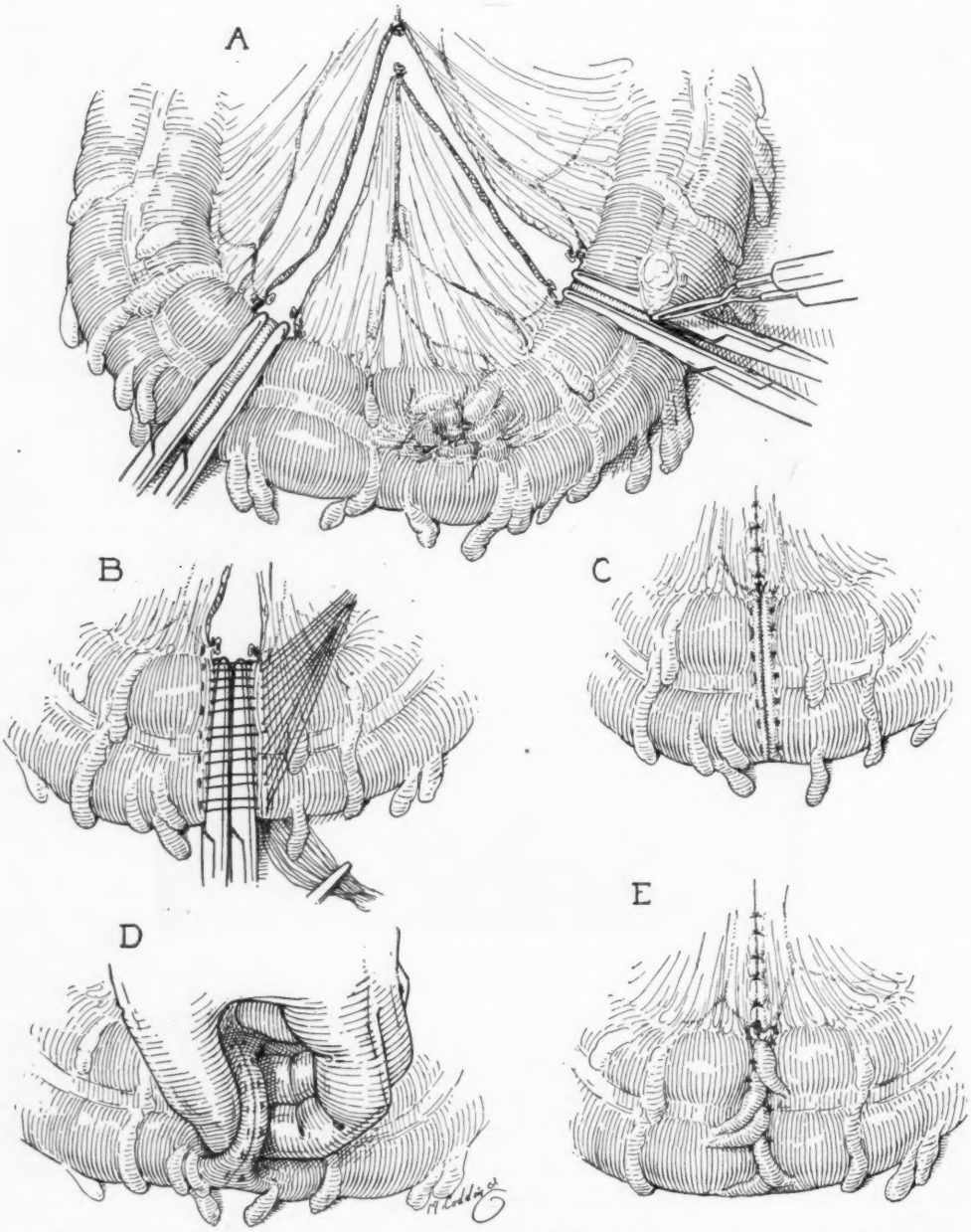

Fig. 2.—*A*, After the bowel has been prepared for resection, excision is made with the actual cautery. *B*, Halsted mattress sutures of silk are placed on one side of the bowel and then on the other. *C*, The clamps are removed and the sutures are drawn up and tied. Extra sutures are placed as necessary or a second row of Halsted stitches may be placed. The mesentery is united with interrupted sutures. *D*, The diaphragm between the two lumina is broken. *E*, The fat tabs are sutured over the anastomosis.

19 to 3 per cent and a reduction in the number of patients with complications from 58 to 25 per cent (see Table I).

TABLE I. COMPARISON BY CASES OF RESULTS IN LARGE BOWEL SURGERY

	NUMBER OF CASES	CASES WITH COMPLICATIONS		DEATHS	
		NO.	PER CENT	NO.	PER CENT
Control group (Miller-Abbott tube and sulfasuxidine *not* used)	78	45	58	15	19
Test group (Miller-Abbott tube and sulfasuxidine used)	36	9	25	1	3

A more significant comparison may be made if cases with similar operative procedures are compared and if the complications are separated into those occurring locally at the site of operation, and those occurring to the patient in general. In Tables II and III are presented the cases of the control and

TABLE II. CASES OF CONTROL GROUP ANALYZED FOR OPERATIVE PROCEDURE AND TYPE OF COMPLICATIONS

	NO. OF CASES	CASES WITH LOCAL COMPLICATIONS				CASES WITH GENERAL COMPLICATIONS						DEATHS	
		INFECTION		DISRUPTION		PULMONARY		PHLEBITIS		MISC.			
		NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Resections with anastomoses	37	16	43	0		5	13	0		1		8†	22
Mikulicz resections	27	7	26	4	15	4	15	0		0		5‡	19
Anterior resections of rectosigmoid*	8	4	50	0		0		2		2		0	
Resections of rectum	6	5	83	0		1		0		1		2§	33
Total	78	32	41	4	5	10	13	2	3	4	5	15	19

*An "anterior resection" removes a segment of rectosigmoid and leaves an end colostomy and an inverted segment of rectum.

†Five patients died of peritonitis; two, of pelvic abscesses and pneumonia; one, of aortic stenosis.

‡Two patients died of peritonitis; one, of septicemia; one, of bronchopneumonia; one, of pulmonary edema.

§One patient died of peritonitis; the other died of pulmonary embolism. Both of them had undergone first stage resections.

test groups divided by type of operative procedure and classifying the complications. The local complications are subdivided into those resulting from infection and from wound disruption. General complications are subdivided into pulmonary complications, phlebitis, and miscellaneous complications. If a single patient had both a local complication and a general complication, each is recorded. In Fig. 3 are compared the results in the strictly comparable groups of cases found in Tables II and III. It demonstrates a *statistically*

TABLE III. CASES OF TEST GROUP ANALYZED FOR OPERATIVE PROCEDURE AND TYPE OF COMPLICATIONS

	NO. OF CASES	CASES WITH LOCAL COMPLICATIONS				CASES WITH GENERAL COMPLICATIONS						DEATHS	
		INFECTION		DISRUPTION		PULMONARY		PHLEBITIS		MISCELLANEOUS			
		NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Resections with anastomoses	32	2	6	3	9	4	13	3	9	0	0	1*	3
Resections of rectum	4	0	0	0	0	1	25	0	0	0	0	0	0
Total	36	2	6	3	8	5	14	3	8	0	0	1	3

*This patient died of massive pulmonary embolism three days after bilateral femoral vein ligation and on the nineteenth day after second stage, right colectomy; a primary ileotranversecolostomy had been done two weeks prior to the colectomy.

TABLE IV. DISTRIBUTION OF COMPLICATIONS IN CONTROL GROUP*

	LOCAL COMPLICATIONS					GENERAL COMPLICATIONS					
	WOUND INFECTION	ABSCESS INTRAPERITONEUM	PERITONITIS	WOUND DISRUPTION	MISCELLANEOUS	ATELECTASIS	PNEUMONIA	INFARCT	MASSIVE PULMONARY EMBOLUS	PHLEBITIS	MISCELLANEOUS
Resections and anastomoses	P-9 S-4	P-1 S-1	P-6	0	0	P-2	P-2	P-1	0	0	P-1 (death due to aortic stenosis)
Mikulicz resections	P-4 S-2	0	P-3	P-4	P-1 (gangrene proximal loop)	P-1	P-3	0	0	0	0
Anterior resections of rectosigmoid	P-1	P-3	0	0	0	0	0	S-1	0	P-2	P-2 (two cases cystitis)
Resections of rectum	P-4 S-1	S-1	P-1	0	0	0	P-1	0	0	0	P-1 (bacteremia)

*If a patient had two local or two general complications both are recorded, the more important as primary "P" and the less important as secondary "S."

TABLE V. DISTRIBUTION OF COMPLICATIONS IN TEST GROUP*

	LOCAL COMPLICATIONS					GENERAL COMPLICATIONS					
	WOUND INFECTION	ABSCESS INTRAPERITONEUM	PERITONITIS	WOUND DISRUPTION	MISCELLANEOUS	ATELECTASIS	PNEUMONIA	INFARCT	MASSIVE PULMONARY EMBOLUS	PHLEBITIS	MISCELLANEOUS
Resections and anastomoses	P-2	0	0	P-3	0	P-4	0	0	0	P-2 S-1	0
Resections of rectum	0	0	0	0	0	P-1	0	0	0	0	0

*If a patient had two local or two general complications both are recorded, the more important as primary "P" and the less important as secondary "S."

*significant** reduction in complications due to local infection from 43 to 6 per cent, and the statistically significant reduction in mortality from 22 to 3 per cent. It is apparent that the decrease in infection is greater than the decrease in mortality. This effect would be expected because factors may enter into the mortality rate which are not affected by either intestinal suction or sulfasuxidine. Tables IV and V present a further analysis of the data in Tables III and IV.

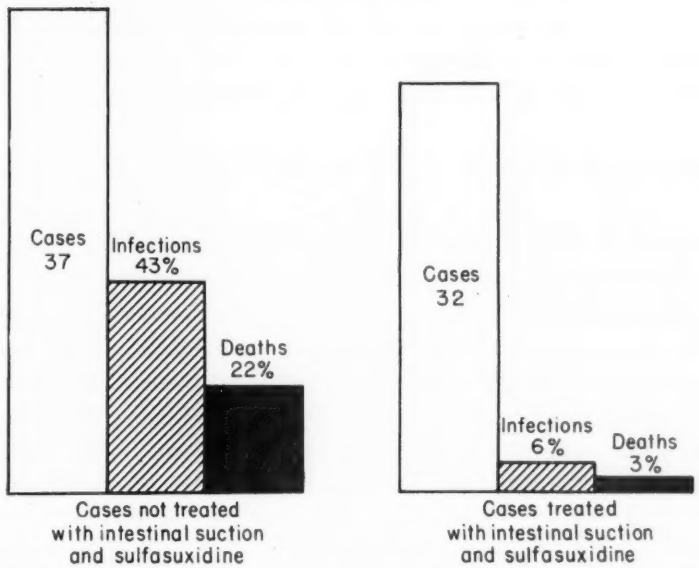

Fig. 3.—Results in large bowel resections and anastomoses with and without intestinal suction and sulfasuxidine.

The apparent increase in wound disruption in the test series of cases cannot be shown to be of statistical significance. It is probably apparent because in the control group of cases those patients who were in a poor nutritional state were chosen for Mikulicz procedures rather than resection and primary anastomosis. Table II shows a higher incidence of wound disruption in the Mikulicz resection group.

The apparent increase in the complication of phlebitis is also not enough to be of statistical significance, even though the frequency of the diagnosis has increased in the last two years because of the greater emphasis on searching for the symptoms and signs of early phlebitis.

DISCUSSION

It appears that the use of succinylsulfathiazole and intestinal suction is a significant contribution to surgery of the colon. Intestinal suction spares the patient the risk of colostomy and colostomy closure; and the succinylsulfathiazole makes the major operative procedure safer, primarily because it produces such marked reduction in the incidence of postoperative local infection. However, we wish here to state our agreement with the opinion of many others that the

*In comparing the percentage change in any two comparable series of cases, the percentage differences must be greater than twice the "standard error of the difference" if the percentage change is to be of statistical significance. The standard error of the difference (S.E.D.) is derived from a formula which takes into account the percentages involved and the number of cases in each group. The change in infection rate above is 4 times the S.E.D. and the change in mortality rate is 2.5 times the S.E.D.

$$\text{S.E.D.} = \sqrt{\frac{\text{Percentage A} \times (100 - \text{Percentage A})}{\text{No. of Cases in Series A}} \text{ plus } \frac{\text{Percentage B} \times (100 - \text{Percentage B})}{\text{No. of Cases in Series B}}}$$

primary requirement in surgery of the colon is a gentle, accurate, and dependable surgical technique. Without this, no adjuncts to surgery can be of any real value.

CONCLUSIONS

A series of 114 cases of large bowel resections was studied. The general preoperative and postoperative care was the same in all except that in the test group (thirty-six cases) preoperative succinylsulfathiazole and preoperative and postoperative intestinal suction were used. In the control group (seventy-eight cases) primary colostomy without chemotherapy was the routine in resections with restoration of continuity.

The Mikulicz type of resection was not required in any cases of the test group.

The following data are of statistical significance in the comparison of the two groups.

1. The gross incidence of complications was reduced from 58 to 25 per cent.
2. The gross mortality was reduced from 19 to 3 per cent.
3. When similar operative procedures (resections and anastomoses) are compared, it is found that the incidence of postoperative infection is reduced from 43 to 6 per cent and the mortality is reduced from 22 to 3 per cent.

The use of intestinal suction and succinylsulfathiazole in the preoperative and postoperative care of patients who undergo large bowel resections has a definite effect in reducing the incidence of postoperative infection and mortality.

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THE TREATMENT OF ADVANCED AND INOPERABLE CANCER

A Résumé of Current Trends Based on a Review of the Literature and Analysis of Personal Case Experiences

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INTRODUCTION

THE attitude of the medical profession, as well as the general public, concerning the efficacy of cancer therapy has been one of disheartening pessimism. Numerous reports of five- and ten-year cures in many malignant growths have recently moderated this tendency. Knowledge of similar remarkable advances achieved in the palliative management of advanced and ineradicable cancer is insufficiently well known. Chronic diseases, such as hypertension, nephritis, diabetes, thromboangiitis, rheumatic endocarditis, and coronary sclerosis, all likewise incurable, are accepted with relative equanimity by both patient and physician. Therapy in conjunction with skillful implantation of a cheerful outlook toward their illness has supplanted the dread abandonment which was the lot of these victims only two and three decades ago. Equivalent results with respect to patient comfort and longevity in the therapeusis of many incurable neoplasms warrant adoption of a more optimistic approach. The terminal stages of cardiac and renal disease are no less difficult to face than those of cancer, yet to relegate all patients with early cardiac and nephritic illness to the category of irreclaimables when prolonged intervals of comfortable and fairly active existence can be achieved would exactly parallel what is too often offered the cancer patient at an analogous stage.[53]

In cancer salvage therapy much can be accomplished by radiological and surgical methods. The patient can be promised a minimum of disability and in a certain small minority, treatment may result in cure. Resurgence of interest in this often neglected field is resulting in the accumulation of a large body of data which when given critical statistical evaluation should lead to improved end results. Until research provides cancer controls of established certainty, it is the responsibility of the doctor to utilize present-day knowledge in this province of cancer to the fullest.

SCOPE OF THE PROBLEM

This paper is concerned primarily with the care of the patient with advanced cancer, inoperable at least in the sense that definite possibility of cure cannot be assured. Radical extirpative surgery and radiation have resulted in improved curative results, here briefly mentioned, of cancer of the breast, colon, rectum, skin, uterus, stomach, kidney, and larynx and to a lesser degree in cancer of the lung, esophagus, and bladder.[25, 50, 52] The progressive role of public health education in minimizing factors producing unnecessary delay in the treatment of cancer is likewise beyond the immediate scope of this paper.

Roughly less than 15 to 20 per cent of all patients with malignant lesions ultimately achieve the status of "five-year cure."[29, 49] Epitheliomas of the

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head, neck, bladder, and cervix and less frequently carcinomas of the esophagus, colon, rectum, prostate, and breast by virtue of their relatively early symptomatology may present themselves at a stage where cure is possible. The majority of other malignancies are not as often recognized at an early enough stage so that cure can be expected.[11, 15, 44, 45, 50] It can be estimated then that 80 per cent of all cancer patients, excluding small epitheliomas, will either primarily or secondarily require palliative medical care.[29, 49, 61] Since in any given year there are approximately one-half million cancer patients in the United States,[22] some 400,000 individuals are prospective candidates for such treatment. Viewed in this light the problem is one of major significance and the potential extension of life and comfort is tremendous.

THE STATUS AND CLASSIFICATION OF THE PATIENT WITH ADVANCED AND INOPERABLE CANCER

In addition to the local, regional, and distant spread of the primary neoplasms, two other major factors influence the curability of the lesion: (1) concomitant illness and (2) physical infirmities of advanced age. It must be emphasized, however, that advanced age of itself does not exclude the application of radical curative or palliative procedures in the relatively vigorous patient. Given proper preparation and follow-up care, the elderly may tolerate such therapy admirably.[1, 59, 68] Infection not only serves as a further toxifying agent but it also appears to stimulate the active spread of the neoplasm.

A working classification into groups of the more usual advanced cancer cases is of importance in bringing into focus the dominant problems encountered and the symptoms to be ameliorated.[61]

I. *Head and Neck Group.*—The head and neck group consists predominantly of epitheliomas and constitutes some 17 per cent of all malignancies.[2, 3, 15] Since even the uncontrollable cases in this division are apt to be slow-growing, proper palliation has much to offer. Frequently growth progresses regionally, often resulting in large open ulcerations and hemorrhage; osteomyelitis of underlying bone; destruction of oropharyngeal structures with dysphagia; or involvement of the larynx, often by massive enlargement of cervical lymphatics, with resultant dyspnea.[2, 3, 8] Carcinoma of the esophagus, characterized primarily by dysphagia, is also considered here. The relatively few tumors in this area which metastasize generally present essentially the features to be described here.

II. *Abdominothoracic Group.*—The abdominothoracic group is best considered under several subheadings grouped according to their disseminative tendencies. Treatment of their symptoms require similar palliative procedures despite the widely varying natures of the primary neoplasm.[40, 43, 61, 69, 73, 74]

A. *Generalizing cancers:* The majority of advanced cancers of the breast, lung, kidney, prostate, and ovary, constitutes almost 30 per cent of all cancers. They tend to metastasize to the osseous systems, lungs and pleura, liver and peritoneum, kidney and adrenals, and brain in roughly that order.[23, 40, 43, 69, 73, 74] In some 15 per cent of cases metastases, for some little understood reason, appear clinically limited to the bones for a prolonged interval.[6, 21, 27, 73] Here pain in the spine, pelvis, and extremities, or of a radicular nature, and pathologic fractures are our main concern. Hepatic, pulmonary, adrenal, and uncommonly renal insufficiency, singly or in combination, may ensue, secondary to parenchymal replacement by tumor tissue.[69] Surprisingly, patients with known lung and liver involvement may maintain active and useful existences

for periods up to two to three years, rarely longer. Advanced intracranial involvement dictates that measures be limited to securing maximum relief of pain and rest. This is also true in the terminal phases of massive liver, peritoneal, lung, and pleural infiltration. Ascites and pleural effusion, however, may ensue long before the patient's condition warrants discontinuance of supportive measures. Jaundice in this group fortunately comes late, as a rule, since it is usually the result of periportal invasion. Cancers of the breast frequently present the specific problem of lymphedema and infiltration of the chest wall, axillary and supraclavicular glands, brachial plexus, and subclavian vessels.[27, 31, 55] Metastases to any sensory nerves may result in agonizing and long-continued pain.

B. *Intermediate cancers:* Over 30 per cent of malignancies are included in the group of intermediate cancers. Carcinoma of the stomach, colon, and rectum often generalizes late and in somewhat different fashion. Hepatic and pulmonary involvement are apt to be less massive, except for anaplastic gastric cancers.[43, 69] Extension to surgically inaccessible regional lymphatics may be the only factor interdicting curability. Instances of isolated enterostomy site recurrences occur sufficiently frequently to be given special consideration. Cancer of the pancreas may produce distressing jaundice by compression or, more commonly, by invasion of the common bile duct. Retroperitoneal extension productive of nerve root pain may be encountered early in gastric and pancreatic malignancy.[37, 71] Malnutrition, nausea, vomiting, intestinal obstruction, diarrhea, and tenesmus may all develop at a stage where their relief may provide a protracted interval of comfort and even activity for the sufferer. These lesions tend to widespread invasion of the parietal and visceral peritoneum, which results in multiple and intractable intestinal obstruction.[40, 69, 74]

C. *Localizing cancer:* Cancers of the uterus, cervix, bladder, and external genitals comprise approximately 18 per cent of cancer cases, the great majority of which are pelvic epitheliomas. Extension occurs relatively late and is often limited to local invasion and spread to the regional lymphatics. The major factors operating against curability here are inaccessibility of involved pelvic fascial planes and deep-seated pelvoinguinal lymphatic structures; also there is a tendency to conglomerate involvement of pelvic organs or so-called "frozen pelvis." Cancer of the cervix and bladder often spreads in such fashion as to occlude the ureters, leading to hydronephrosis and pyelonephritis, which if unchecked will result in uremia. The less anaplastic prostatic lesions often take this same course. Vesicorectal, rectovaginal, and vesicovaginal fistulas may be the distressing end result. On occasion urinary retention may occur, although an agonizing frequency is the more common complaint. At times rectal involvement may cause either tenesmus or obstructive symptoms. Massive hemorrhage may occur in cervical and less frequently in rectal lesions.[69]

III. *Sarcomas.*—Melanosarcomas, osteogenic and unspecified sarcomas, and lymphoblastomas in the aggregate come to but 5 per cent of all malignancies. Advanced cases present most often mediastinal, pulmonary, and hepatic metastases, bulky invasion of inguinal para-aortic, or cervical lymphatics, and on occasion a ponderous ulcerated infected primary focus. Terminal cases often present a dissemination as generalized as that of cancer of the breast.[43]

PROBLEMS OF TREATMENT IN ADVANCED CANCER

By now reviewing briefly the pathology of ineradicable cancer, the symptoms requiring palliation become clarified. Therapeutic programs can be facil-

itated by the schematic presentation of the most common problems for which worth-while remedial measures can be carried out.

I. *Head and Neck Group.*—Intractable dysphagia and dyspnea, extensive ulcerations or fungating lesions associated with hemorrhage, osteomyelitis and radiation necrosis, osteochondritis, massive cervical lymphadenopathy, pain mediated by trigeminal and upper cervical nerves, malnutrition.

II. *Abdominothoracic group.*—

A. *Generalized metastases:*

(1) Osseous: Pain in skull, spine, pelvis, extremities. Pathologic fractures, most commonly of humerus, femoral shaft and neck, thoracolumbar spine and pelvis.

(2) Lung and Pleura: Pain, cervical and thoracic, innervated by cervical trunks, intercostal and phrenic nerves. Pulmonary insufficiency due to lung replacement or atelectasis; pleural effusion.

(3) Peritoneum, Liver, and Adrenals: Frequently leading to hepatic and suprarenal insufficiency. Massive ascites; abdominal pain mediated by autonomic nervous system and lower thoracic nerves. Malnutrition, nausea, vomiting, diarrhea, and obstipation.

(4) Somatic and Peripheral Nerve Infiltration: Brachial plexus and upper intercostal nerve pain in cancer of breast and pulmonary apices. Thoracolumbar spinal nerve root pain in primary or secondary retroperitoneal growths. Lymphedema and infiltration of chest wall, axillary, and supraclavicular glands, primarily in malignancies of mammary origin.

B. *Localized metastases:*

(1) Abdominal: Large fungating lesions of gastric wall, cecum, and colon causing obstructive symptoms, diarrhea, or interference with nutritive absorption; recurrences about enterostomy or enteroenterostomy stomas. Jaundice due to compression or invasion of ductus choledochus, most commonly in cancer of head of pancreas.

(2) Pelvic: Pain along autonomic and lumbosacral nerves. Rectosigmoid obstruction. Rectal, vesical, and vaginal fistulas. Tenesmus and urinary urgency. Hemorrhage. Ureteral obstruction, pyelonephritis, and uremia.

(3) Extremities: Elephantiasis of extremities with bulky, ulcerating, infected bone-invading primary tumors, associated with regional lymphadenopathy. Pain along peripheral nerves of extremities.

METHODS OF TREATMENT OF ADVANCED AND INOPERABLE CANCER

Radiation Therapy.—Limitation of growth, diminution in size, control of secondary infection, and on occasion total ablation of the primary lesion or of individual metastases are the major objectives of roentgen therapy. In such tumors as the lymphoblastomas, Ewing's myeloma, and epitheliomas of the skin, pharynx, or cervix, radio-sensitivity or accessibility of the primary or secondary lesion contributes to often dramatic results.[15, 52, 56] Local and lymphatic recurrences of breast cancer may frequently respond to intensive radiation.[7, 27, 31, 55] The interstitial use of radium or radon in squamous-cell carci-

noma, rectal and bladder malignancies, or the secondary deposits of mammary cancer may be rewarded by arrest or destruction of the lesion. Radiation therapy of laryngeal,[17] esophageal,[62] bronchogenic,[46] and gastric[58] cancer has been productive of significant palliation. Advanced secondary cervical lymphadenopathy[3, 66] and the frozen pelvis may be benefited to some degree by x-ray treatment. The technical details of radiation therapy cannot be described here, but adequate tumor lethal doses whether by massive or fractional application must be administered.[35] Supervoltage apparatus does not appear to offer increased advantage thus far.[30, 70] Contact therapy, however, has proved itself valuable in dealing with numerous surface lesions, for example in attacking multiple subcutaneous breast cancer metastases.[31] Recent studies have indicated the palliative value of the oral or parenteral administration of radioactive phosphorus in lymphosarcoma and in some cases of chronic myelogenous leucemia and multiple myeloma.[41] Considerable promise for improved results with x-ray and radium treatment seems definite as research in this field progresses.

Bone metastases, particularly secondary to carcinoma of the breast,[31] often respond to radiation in spectacular fashion, allowing even three- to five-year periods of active relatively pain-free survival.[6, 21, 42] Rarefying osteoclastic lesions are replaced by a calcifying or sclerosing osteoblastic process restoring osseous strength and stability. Pathologic fractures may heal sufficiently to permit normal gait and weight-bearing. Treatment of the latter may be usefully augmented by traction, frames, braces, or cast application, and in selected cases by the use of bone pins and plates for fixation. The radiation sensitivity of osseous metastases varies, but does not appear to correspond exactly with that of the primary growth.[56] Carcinoma of the breast, testes, and thyroid is relatively quite radiation-resistant as a primary lesion, but radiation-sensitive as a secondary skeletal deposit.[56] Metastatic cancers of the prostate, bladder, cervix, oropharynx, lung, and intestine, on the other hand, generally respond less satisfactorily.[21] Hypernephroma produces bone secondaries that are quite insensitive to x-rays.[33] Lymphoblastomatous, leucemic, and myelomatous infiltration of bone is frequently greatly relieved by irradiation, particularly in the initial courses of therapy. Isolated pulmonary, pleural, and mediastinal metastases of the more radiation-sensitive tumor types have been known to recede with therapy.[70] Lastly, the ascites due to peritoneal implantation by ovarian carcinoma may respond favorably.[21] Here the fluid is not resorbed but the interval between tappings is often prolonged.

Surgery.—Ligation of the carotid arteries for the control of hemorrhage from advanced head and neck lesions is a commonplace procedure. This may permit further therapy of the primary tumor. Resection of involved and necrotic facial bones or mandibles has been followed by as much as several years of relatively comfortable activity in some previously desperate cases.[8] Since the operation is attended by a relatively low mortality and the tumor is often of a slow-growing type, block dissection of cancerous cervical lymph glands may have much to offer the patient in selected cases.[3, 24, 66] Many surgeons advocate the excision, by scalpel or electrosurgery, of most large ulcerating or fungating primary or secondary lesions and have demonstrated that a relatively clean granulating surface, in some instances suitable for skin grafting, contributes much to patient comfort and is attended by less pain.[13, 14, 40, 57, 75] Marked reduction of great and hitherto impenetrable tumor bulk, as of face[14] or breast,[60] may render irradiation more effective. Electro-

coagulation of large rectal and bladder lesions may give similar temporary improvement.[5, 75] Denuded raw surfaces kept clean and granulating under pliofilm or paraffin gauze dressings are tolerated better than advanced infected ulcerative lesions.

During exploratory laparotomy the practice of resecting primary gastric or large bowel lesions, when feasible, in the presence of early hepatic involvement postpones the advent of discomfort considerably, as a rule. Case reports of actual resection of isolated hepatic and other intra-abdominal secondary implantations with good results are becoming less great rarities.

Circumventing operations for the relief of dysphagia and obstructive dyspnea may establish temporary rehabilitation of the patient. Low tracheotomy in laryngeal and hypopharyngeal cancer or for massive cervical metastases may facilitate palliative radiation therapy as well as contribute greatly to the comfort of the patient. Tubovalvular gastrostomy may counteract for many months or longer the dysphagia of oropharyngeal cancer or the obstruction of esophageal neoplasms. In large indolent gastric cancers, jejunostomy for feeding purposes may be of some avail. These procedures should not be deferred until the emaciated condition of the patient prejudices the outcome of the operation.

Massive pleural effusion and ascites should be tapped as frequently as the dyspnea and distention are produced. Instances of survival for several years with multiple abdominal or thoracic paracentesis is known. The use of mercurial diuretic, for example, salyrgan or mercupurin, has never lessened the need for puncture[67] in our experience.

Colostomy, when indicated as palliative procedure for the relief of such symptoms as obstruction by neoplasm, diarrhea, tenesmus, or rectovesical or rectovaginal fistulas, is preferably carried out as a defunctionalizing procedure, completely isolating the lower colonic segment. This allows further surgical, electrosurgical, or radiological attack upon the primary lesion as well as minimizes distress. At times short-circuiting operations, notably ileotransversostomy, for unresectable intestinal obstructive new growths may be resorted to. Tumor recurrences about the colostomy stomas, along with their areas of regional lymphatic spread, are occasionally secondarily resected with good results. Jaundice in carcinoma of the bile duct and pancreas is at times effectively palliated by choledochojejunostomy. Cystoscopic ureteral dilation and drainage, frequently repeated, is occasionally followed by intervals of well-being in pyelonephritis secondary to cancer of the cervix. Ureterostomy, preferably by implantation into the colon, and suprapubic cystotomy may do much to alleviate the suffering of patients with cancer of the cervix, bladder, and prostate.

A hitherto greatly neglected palliative application of surgery, which has only recently come into its own and has been given impetus by the increasing life span afforded certain categories of incurable cancer patients with newer forms of treatment, is the operative relief of pain.[9, 10, 16] Section or anesthetic infiltration of individual branches of the trigeminal nerve or alcohol injection of the gasserian ganglion are particularly effective and simple procedures too often neglected in advanced face lesions. Glossopharyngeal and cervical alcohol nerve block have a more limited but nonetheless definite field of usefulness. Intramedullary tractotomy has recently been reported for the relief of unilateral face and neck pain in these cases.[71, 72]

Interruption of sympathetic fibers for the control of intractable pain from various abdominal organs has repeatedly proved its worth. Thus, paraverte-

bral alcohol infiltration to destroy the right lower six thoracic sympathetic ganglia and rami can often give satisfactory relief for the duration of their lives to patients with advanced metastatic carcinoma of the liver.[37, 72]

Although all uncomfortable sensations may not be obviated by this approach which is calculated to block the newly charted visceral afferent pathways, paravertebral sympathetic block of several segments of the thoracolumbar chain below the level of the sixth thoracic may provide a prolonged and welcome respite from the greater part of pain arising from inoperable cancer of the stomach and intestines. In selected patients splanchnicectomy and thoracolumbar sympathetic ganglionectomy may be attempted. Removal of the upper lumbar ganglia is of value in pain of renal and ureteral origin. Presacral neurectomy[36] by interrupting the sacral parasympathetic nerves ameliorates greatly the pain of rectal or bladder neoplasms. Where pain is due to a retroperitoneal invasive process, posterior rhizotomy or spinothalamic tractotomy, that is, anterolateral chordotomy successfully alleviates suffering.[71, 72] The intrathecal administration of alcohol particularly where lesions are widespread, negating a segmental approach for nerve impulse interruption, can often be depended upon to control pain for several weeks or months by its degenerative action on the posterior rootlets when the proper technique is followed.[73] Post-mortem examination has several times confirmed the relatively selective localization of the action of alcohol so introduced into the spinal column to the dorsal sensory nerve roots.[54] In the event of the initial failure of alcohol, or as more recently advocated ammonium sulfate solution,[37] administered intraspinally, it may be repeated or neurosurgery may be carried out. Some degree of bladder and bowel incontinence may follow these injections, but to a large extent this is transitory. On occasion a reactive alcoholic neuritis may ensue, in which case pain can be ameliorated by return to the analgesic and narcotic medications previously depended upon. Accurate neurologic localization of the pain zones and pathways prior to instituting these forms of therapy is rewarded by maximum benefits with minimal interruptive techniques.[37, 72] Stimulated by its use in the edema of thrombophlebitis, cervicothoracic sympathetic block together with elastic adhesive bandaging has given favorable results in several of our cases of lymphedema of the upper extremity following radical mastectomy, and sympathectomy may be advisable.

Formidable surgical procedures in patients with incurable malignant growths have the sole object of mitigating or forestalling unbearable agony where the sufferer can, in the event of survival, look forward to a period of months or years free from pain. Operative death rates of as high as 10 per cent, the maximum generally to be anticipated from the procedures detailed, are not as deterrent as in elective general surgery, since where extreme and prolonged suffering cannot be palliated, a surgical mortality cannot be construed as the same unwelcome outcome. However, the once enormous risks entailed in operating on patients with advanced cancer can be greatly curtailed by thoroughgoing preoperative and postoperative care.[12, 34, 38, 59]

Surgical sterilization by ovariectomy and orchiectomy has had many recent favorable reports in advanced mammary and prostatic cancer, respectively.[4, 32, 47, 51, 65] Most workers stress the production of temporary clinical arrests and the apparent augmentation of irradiation effects on secondary skeletal lesions. Radiation castration in conjunction with hormonal therapy[26] may prove to be effective in the light of current studies. Sporadic instances of five-year apparent cures in patients with bone metastases treated by castration and irradiation supplemented by endocrine administration have been seen.

Pharmacologic Therapy.—Foremost in importance among the medications given in advanced cancer are the analgesics. A cardinal principle to be followed in their administration is the postponement of narcotic utilization until the decreased potency of other drugs counterweighs the disadvantages of potential addiction. At the outset salicylates and barbiturates are generally adequate, later to be supplemented by codeine, which rarely causes serious habituation. Small doses of morphine, pantopon, or dilaudid may prove effective for long periods in the majority of cases. Whenever possible, relief of intractable regional pain by alcohol nerve block or neurosurgery is preferred to the deleterious effects of constant dependence on large doses of narcotics. On the other hand, since the comfort of the patient is of paramount importance, opium derivatives or analogues and sedatives should not be withheld when other measures are no longer of avail. Recently demerol[76] has been found to induce satisfactory pain relief, in some instances, without many of the well-known physiologic disadvantages of the opiates. For oropharyngeal lesions, local anesthetics, such as orthoform or cocaine are helpful. Numerous medicaments have been sponsored as panaceas for the pain of advanced malignancies, the majority of which are the subjects of conflicting descriptions concerning their usefulness. Cobra venom falls into this class of substances which cannot be said to offer uniform palliation. Other preparations which have had considerable vogue but seemingly fail in the majority of cases are colloidal lead and gold solutions and Coley toxin.[67] Recent trial of H 11 and heptaldehyde has been relatively fruitless.

The need of supportive measures in the treatment of progressive malignancy should never be overlooked. Malnutrition, dehydration, disturbance of acid-base equilibrium, and cachexia may be combated by oral, tubal, and parenteral administration of nutritive fluids and electrolyte solutions. Care must be taken to guard against overloading the circulation in the frequently concomitant cardiovasculorenal degenerative diseases.[12, 59] Specific metabolic deficiences leading to anemia and hypoproteinemia seem to characterize many forms of cancer.[59] High caloric diets, protein hydrolysates, liver concentrates, and hematinics are thus of great value, and serve to lessen weakness, fatigability, and susceptibility to infection. Similarly indicated are various polyvitamin preparations, since avitaminosis of various types is generally encountered in these patients and anorexia is commonplace. The vitamins may serve to control nausea and vomiting. Sedation judiciously administered in conjunction with antispasmodics and alkali carminative powders may also help. In gastric carcinoma with attendant achlorhydria, dilute hydrochloric acid and pepsin may be beneficial. Gastric lavage will often terminate otherwise unpalliated vomiting episodes. Distressing diarrhea, likely to be characteristic of enterostomy and enteroenterostomy cases, responds usually to careful dietetic management supplemented by such preparations as kaolin, pectates, magnesium and aluminum hydrogels, and paregoric. Anodyne and antispasmodic suppositories have also their useful indications.

Endocrine derivatives and synthetics as previously mentioned[20, 26] now loom large in the palliation of various neoplastic diseases. Thus, testosterone and more lately diethylstilbestrol, especially in postmenopausal cases of metastatic breast cancer, appear to bring about temporary improvement in some cases.[55b] Stilbestrol in the opinion of some workers has supplanted orchiectomy as a treatment of choice in cancer of the prostate with osseous dissemination.[20] Adrenal medullary cortical extracts and hormone synthetics in con-

junction with the administration of saline solution is indicated[63] where a secondary Addison syndrome supervenes.

The local treatment of foul infected ulcerating or fungating lesions, in addition to electrosurgical excision and radiation, has profited by several new techniques. Systemic use and local application of the sulfonamides or penicillin may control infection to a noteworthy extent. Zinc peroxide, azochloramid, and

Fig. 1 (Case 2, M.B.).—Basal-cell carcinoma of nose and lip, recurrent and advanced.

Fig. 2 (Case 3, A.R.).—Squamous-cell carcinoma of forehead, scalp, and eyebrow; osteomyelitis of frontal bone.

eucupine ointment are of adjuvant worth in this respect.[28, 64] Such old standbys as Dakin's solution, potassium permanganate, and gentian violet may be advantageously employed. Zinc oxide, kaolin, paraffin suspensions, and bronze-aluminum powder may counteract the surface excoriations produced by irritating fistula, colostomy, and ureterostomy discharges. Decubitus ulcers should be prevented by such means as maintaining adequate blood protein levels, and avoidance of pressure by the use of inflated rubber cushions, squares of sheepskin, frequent changes of bedding and position, and skin massage.

Physical Therapy.—Although cryotherapy is no longer considered of much value in the palliative treatment of cancer, amputation using local refrigeration anesthesia is worth while in selected cases. Occasional employment of such modalities as diathermy and moist heat may afford relief, but as a rule physiotherapy has little to offer in this field. Diathermy and fever therapy have been reported as promising sensitizing agents augmenting the effect of irradiation. This work, however, is still at the experimental stage.[77]

Fig. 3 (Case 6, J.D.).—Squamous-cell carcinoma of lip, recurrent, with extension to chin and gingiva.

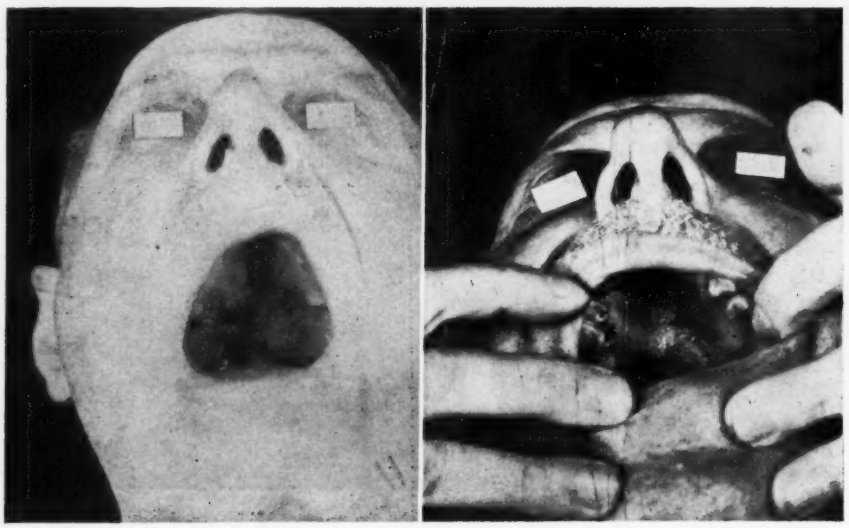

Fig. 4 (Case 8, J.C.).—Mixed tumor of palate, recurrent, with large ulceration and palatal perforation; patient likewise has prostatic carcinoma with pelvic metastases.

Psychotherapy.—Of paramount importance here are the attitude of the physician and provision of thorough and sympathetic efficient nursing care. Hopelessness will handicap the incentive of the doctor, and lead to his regarding the task as a disagreeable chore. Emphasis on what can be offered the patient in the way of the most comfortable prolongation of life must be kept uppermost in mind and impressed upon the family. The morale of the patient can best be maintained by an optimistic and cooperative approach on the part of both inti-

mates and medical attendants. Although no invariable routine can be recommended, the physician generally does best by not committing himself to the patient concerning absolute incurability and life expectancy. Parrying the inevitable questions and countering with psychically helpful suggestions requires tact, understanding, and patience. Keeping the patient as active and as completely engaged as his physical condition warrants is of inestimable worth. Exceptional individuals are capable of maintaining a philosophic poise and admirable equanimity given full realization of the gravity of their condition. However, this, too, can be made to endure successfully only when pain and distress are adequately counteracted by judicious therapy.

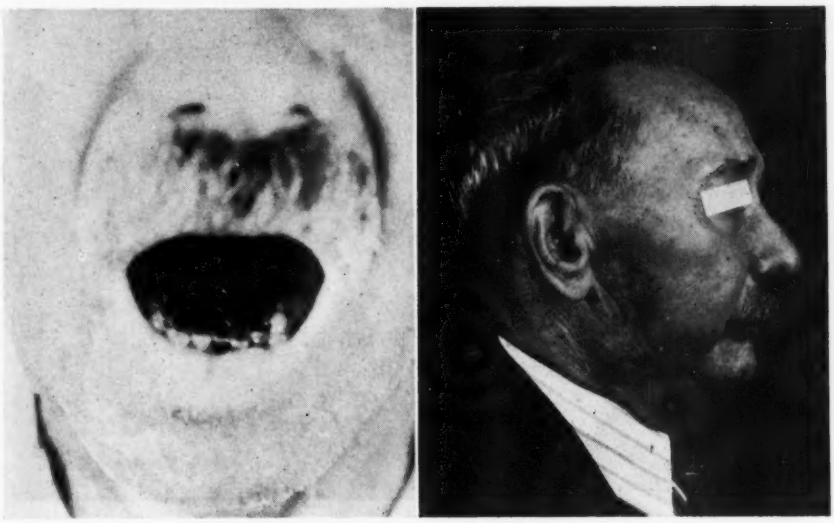

Fig. 5 (Case 9, C.S.).—Squamous-cell carcinoma of floor of mouth; mandibular involvement, cervical metastases.

Fig. 6 (Case 10, W.I.).—Squamous-cell carcinoma of tonsil; involving fauces, soft palate, and posterior pharynx.

CLINICAL REPORTS

Comprehensive reports of end results in a large series of patients given palliative treatments for advanced cancer seldom appear in the literature for sites other than the breast or prostate. Published studies generally are concerned with primarily curable cases and scant consideration is given those

dismissed as advanced beyond this degree. Consequently, valid evaluation of the efficacy of palliative treatment demands the future accumulation of considerable further data. The natural yardstick for the accurate estimation of success in such therapy is the longevity of comparable untreated patients. The tendency to allocate patients too desperately ill for even remedial procedures to control groups must be guarded against.[18, 19, 48]

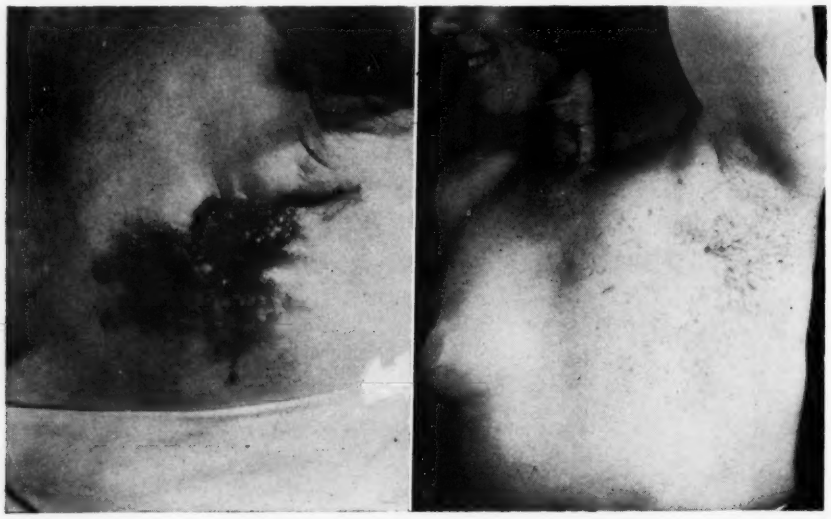

Fig. 7 (Case 17, K.B.).—Adenocarcinoma of breast; advanced ulcerative lesion invading ribs, with metastases to axilla and spine.

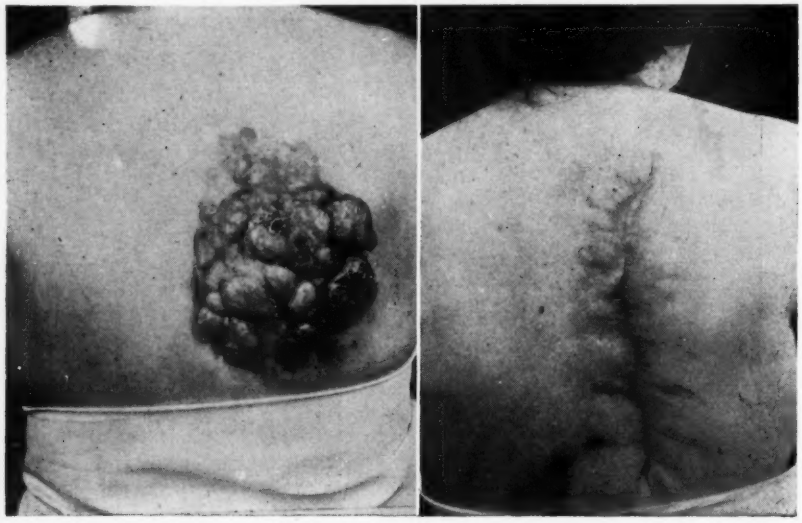

Fig. 8 (Case 25, M.K.).—Neurogenic sarcoma of back; recurrent, ulcerative, and fungating, deeply invasive.

Available clinical experiences do permit one to draw these general conclusions. The duration of life is appreciably longer in treated than untreated groups of patients, and three-year survivals are relatively frequent in the former and rare in the latter. That symptomatic relief can be attained whether or not life is actually prolonged has been amply attested to by many radiologists and surgeons. Moreover, a small unpredictable percentage of cures in apparently irreclaimable malignancies has been reported. Postexploratory withdrawal of supportive therapy from the large group of patients found to be in-

curable is to be condemned. Early postoperative mortalities cannot but discourage other prospective cancer sufferers and in large measure frustrate the public health campaign of education concerning prompt diagnosis and treatment.

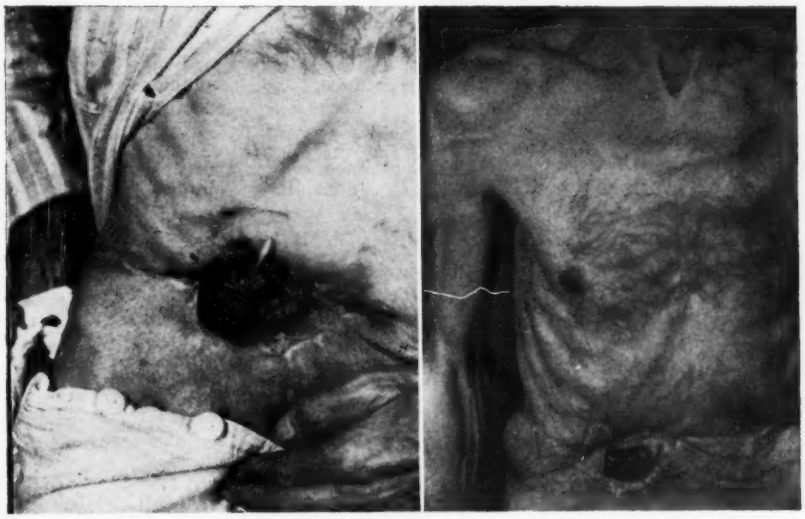

Fig. 9 (Case 32, M.S.).—Adenocarcinoma of sigmoid; multiple recurrences, with prolapse of colostomy stoma.

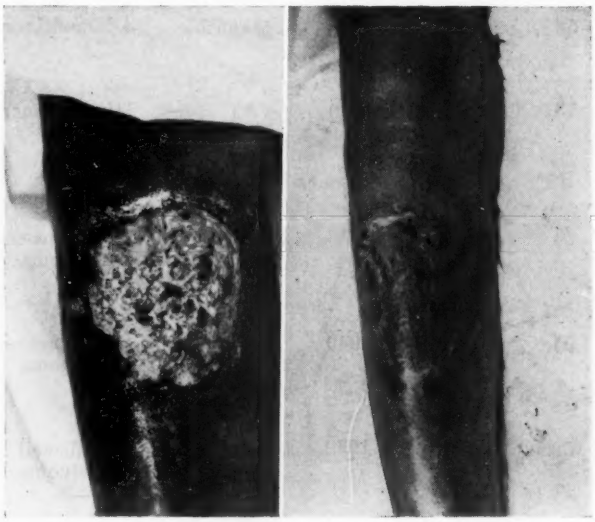

Fig. 10 (Case 41, H.G.).—Squamous-cell carcinoma of leg; recurrent advanced lesion with inguinal ulceration and lymph node involvement.

Selected cases of forty-two patients treated at the Brooklyn Cancer Institute were presented in detail at the 1944 session of the Medical Society of the State of New York as examples of what persistent and intensive therapy might accomplish in lesions of this type. The only cases included were those in which the patients had been initially referred to the institution with advanced and recurrent cancers beyond attempts at cure, who were ambulatory, active, and in relative comfort at the time of presentation. Survival periods range from two and one-half to fourteen years, and average four and one-half years. The cases presented are too small a sample for valid statistical analysis. The patients receiving their initial therapy at Brooklyn Cancer Institute and later requiring secondary treatment are excluded. Similarly, several hundred pa-

TABLE I. DATA ON FORTY-TWO REPRESENTATIVE CASES OF ADVANCED AND RECURRENT CANCER TO BROOKLYN

CASE	PATIENT	AGE (YR.)	SEX	B. C. I. ADMISSION DATE	SITES	PATHOLOGY	STATUS ON ADMISSION TO B. C. I
1	F. L.	43	F	1937	Head, face, neck	Basal- and squamous-cell carcinomas	Recurrent and extensive lesions 1-6 cm. in diameter
2	M. B.	64	F	1940	Face, nose, lip	Basal-cell carcinoma	Recurrent extensive ulcerating lesion 7 cm. in largest diameter
3	A. R.	56	M	1939 (N.Y.C.I.) 1942 (B.C.I.)	Scalp, forehead, eyebrows	Squamous-cell carcinoma	Advanced ulcerating recurrence, invasion and osteomyelitis of frontal bone
4	H. C.	46	M	1937	Lip, chin	Squamous-cell carcinoma	Large recurrent ulceration, spread to submaxillary, salivary, and cervical lymph glands
5	H. E.	63	M	1940	Lip, chin, cheek	Basal-cell carcinoma	Recurrent large ulceration
6	J. D.	61	M	1938	Lip, chin, gingiva	Squamous-cell carcinoma	Recurrent large ulcerating lesion
7	H. S.	53	M	1940	Mandible	Adamantinoma	Floor of mouth and cheek
8	J. C.	73	M	1940	(A) Hard palate	Mixed tumor	Recurrent with large ulceration
					(B) Prostate	Adeno-carcinoma	Pelvic metastases
9	C. S.	60	M	1938	Floor of mouth	Squamous-cell carcinoma	Recurrence, mass of cervical glands fixed to jaw; mandible involved
10	W. I.	51	M	1940	Tonsil, fauces, oral cavity	Squamous-cell carcinoma	Recurrent large ulcerating and fungating lesion
11	W. S.	52	M	1939	Larynx and hypopharynx	Prickle-cell carcinoma	Recurrent advanced extrinsic spread
12	B. F.	58	M	1940	Larynx, epiglottis, base of tongue	Squamous-cell carcinoma	Recurrent advanced ulcerating lesion
13	B. P.	40	F	1940	Thyroid	Adeno-carcinoma	Recurrent neck mass, pulmonary metastases
14	F. C.	35	F	1930	Shoulder, arm	Round-cell carcinoma	Advanced recurrence with involvement of shoulder joint and humerus
15	J. B.	32	F	1940	Breast	Medullary carcinoma	Skin recurrences, generalized osseous metastases including spine, skull extremities, pelvis

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AT PRESENT AMBULATORY, SURVIVING AN AVERAGE OF FOUR YEARS AFTER INITIAL ADMISSION

CANCER INSTITUTE

COMPLICATIONS	PRIOR THERAPY	RADIATION AND RADIUM	SURGICAL PROCEDURES	"SALVAGED" YEARS ACTIVE SURVIVAL	STATUS
Ulceration, infection, skull involvement	Radiation	Repeated courses	Repeated electrosurgical excisions	7	Arrested
Perforating ulceration of nasal cavity, lip, lower orbit	Radiation	Repeated courses	Partial excision and plastic	4	Cure(?)
Hemorrhage, Osteomyelitis, ulceration, infection	Radiation	Repeated courses	Repeated electrosurgical excision at N. Y. C. I. of lesion, frontal bone plastic repair	5	Cure(?)
Ulceration, fixation to mandible	Radiation	Repeated courses	V-Resection lip, block dissection neck, resection submaxillary salivary gland	7	Cure(?)
Ulceration, infection	Radiation	Repeated courses	Dental	4	Cure(?)
Ulceration, infection	Radiation, caustics	Repeated courses	Dental	6	Cure(?)
Displacement of tongue	Radiation, partial excision	--------	Resection mandible	4	Cure(?)
Palatal perforation	Radiation	Repeated courses	Palatal resection and plastic repair	4	Improved
Pain	--------	Repeated courses	Orchiectomy + (stilbestrol)	4	Improved
Ulceration, hemorrhage, necrosis of mandible	Radiation	Repeated courses	Carotid ligation, resection of mandible; block dissection of neck	6	Cure(?)
Ulceration, infection	Radiation	Repeated courses	--------	4	Cure(?)
Dyspnea, dysphagia	Radiation	Repeated courses	Tracheotomy, laryngectomy	5	Cure(?)
Dyspnea	Radiation	Repeated courses	Electrosurgery	4	Cure(?)
Dyspnea	Thyroidectomy	Repeated courses	Repeated excision neck tumor	4	Improved
Elephantiasis, osteomyelitis, ulceration	Radiation, 3 resections	Repeated courses	Disarticulation, amputation	14	Cure
Pathologic compression, fracture thoracic spine	Radical mastectomy, radiation	Repeated courses	Orthopedic	4	Improved

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TABLE I.—CON

CASE	PATIENT	AGE (YR.)	SEX	B. C. I. ADMISSION DATE	SITES	PATHOLOGY	STATUS ON ADMISSION TO B. C. I.	COMP
16	C. K.	71	M	1941	Breast	Adenocarcinoma	Recurrent, large fungating lesion	Ulcera infect
17	K. B.	46	F	1939	Breast	Medullary carcinoma	Advanced ulcerative lesion, metastases to spine, rib	Ulcera Infect
18	M. L.	65	F	1937	Breast	Adenocarcinoma	Advanced bulky tumor with axillary metastases	Indura and a
19	W. W.	63	M	1939	Breast	Adenocarcinoma	Advanced, large fungating tumor involving axillary glands and ribs	Ulcerat infect
20	M. B.	42	F	1940	Breast	Medullary carcinoma	Multiple skin nodules; metastases to skull, pelvis, long bones, ribs	Multipl lesions
21	E. S.	34	F	1941	Breast	Adenocarcinoma	Pelvic metastases; supraclavicular glands	Lymph arm
22	E. R.	23	F	1935	Axilla and chest wall	Neurogenic sarcoma	Extensive ulcerative fungating recurrence	Rib inv
23	M. H.	37	F	1940	Neck	Malignant lymphoma	Involving skull, ribs, cervicothoracic spine, hips, long bones, skin	Pathol fractu
24	L. M.	50	F	1940	Chest wall and ribs	Osteochondrosarcoma	Large recurrent mass in chest wall involving 5th, 6th, 7th ribs	Ulcerat infecti
25	M. K.	52	F	1940	Back	Neurogenic sarcoma	Recurrent extensive fungating lesion from 3rd to 8th rib	Ulcerat infecti
26	J. A.	4 mo	F	1941	Retroperitoneal	Neurocytoma	Advanced, large abdominal tumor	Visceral renal ment
27	M. S.	11	F	1940	Kidney	Hypernephroma	Recurrent large abdominal mass	Extensi periton growth compre
28	S. N.	58	F	1938	Stomach	Adenocarcinoma	Advanced gastric cancer, palpable mass	Extensi conside inopera year b
29	M. K.	58	M	1941	Stomach	Adenocarcinoma	Postlaparotomy, inoperable lesion	Extensi gional
30	J. D.	40	M	1942	Jejunum	Adenocarcinoma	Large papillary lesion	High in obstruc
31	E. G.	64	F	1941	Cecum	Adenocarcinoma	Large peristomal recurrent mass	Ulcerati recurre colosto obstruc
32	M. S.	65	M	1938	Sigmoid	Adenocarcinoma	Extensive multiple peri colostomy and abdominal wall recurrences	Ulcerati infecti colosto obstruc

TABLE I.—CONT'D

COMPLICATIONS	PRIOR THERAPY	RADIATION AND RADIUM	SURGICAL PROCEDURES	"SALVAGED" YEARS ACTIVE SURVIVAL	STATUS
Ulceration, infection	Partial excision	Repeated courses	--------	3	Cure(?)
Ulceration, Infection	--------	Repeated courses	--------	5	Improved
Induration chest and axilla	--------	Repeated courses	--------	7	Arrest
Ulceration, infection	Radiation	Repeated courses	Radical mastectomy	5	Cure(?)
Multiple skin lesions	Radical mastectomy, radiation	Repeated courses	Local recurrence, excisions	4	Improved
Lymphedema of arm	Radical mastectomy	Repeated courses	Paravertebral injection	3	Improved
Rib invasion	Partial excision	Repeated courses	Secondary radical resection	9	Cure
Pathologic fracture hip	Laminectomy, cord decompression	Repeated courses	Orthopedic	4	Improved
Ulceration, infection	Partial excision, radiation	Repeated courses	Secondary radical resection	4	Cure
Ulceration, infection	Excision, radiation	Repeated courses	Secondary radical resection, skin grafts	4	Cure
Visceral and renal displacement	Radiation	Repeated courses	Radical resection	3	Cure(?)
Extensive retroperitoneal growth, renal compression	Partial excision, radiation	Repeated courses	Secondary radical resection	4	Cure(?)
Extensive tumor considered inoperable 1 year before	Radiation	--------	Subtotal gastrectomy	6	Cure
Extensive regional spread	Laparotomy	Repeated courses	--------	3	Improved
High intestinal obstruction	Gastroenterostomy, radiation	--------	Radical enterectomy	2½	Cure(?)
Ulceration, recurrence, colostomy obstruction	Mikulicz type resection	Repeated courses	Secondary radical resection	3	Cure(?)
Ulceration, infection, colostomy obstruction	Obstructive resection	--------	Repeated electrosurgical excisions and colostomy revision	6	Arrested

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TABLE I—CONT

CASE	PATIENT	AGE (YR.)	SEX	B. C. I. ADMISSION DATE	SITES	PATHOLOGY	STATUS ON ADMISSION TO B. C. I.	COMPL
33	O. L.	50	M	1940	Colon, splenic flexure	Gelatinous adeno-carcinoma	Post laparotomy, massive perforating tumo	Intestir obstru toxem
34	A. G.	55	F	1942	Sigmoid	Adeno-carcinoma	Large peristomal recurrence with involvement of inferior mesenteric glands	Colosto obstru
35	C. N.	29	F	1936	Rectum	Adeno-carcinoma	Large postoperative recurrence	Postrad frozen
36	H. K.	38	F	1939	Ovary	Papillary cystadeno-carcinoma	Postlaparotomy for large extensive abdominal mass	Frozen intesti obstru
37	R. C.	55	F	1938	Cervix	Squamous-cell carcinoma	Recurrent extensive lesion, Schmitz IV	Frozen pyelon pathol fractu
38	M. F.	61	F	1938	Cervix	Squamous-cell carcinoma	Extensive lesion, Schmitz IV; metastases to pelvis and spine	Frozen pyelon pathol fractu and h
39	K. E.	59	F	1937	Vulva	Squamous-cell carcinoma	Recurrent extensive ulcerative lesion, both labia and perineum	Ulcerat infecti
40	M. S.	64	M	1942	Prostate	Adeno-carcinoma	Generalized rarefying skeletal metastases, especially pelvis, skull, spine, long bones	Pain, v
41	H. G.	31	F	1941	Leg	Squamous-cell carcinoma	Large recurrent fungating lesion, massive involvement of groin and inguinal nodes	Ulcerat infecti
42	J. S.	44	M	1940	Foot	Malignant melanoma	Large local recurrence with massive involvement popliteal, inguinal, and pelvic para-aortic glands	Ulcerat infecti

tients in whom satisfactory palliation of several years' duration had been achieved, but who had died or where incapacitated by malignant disease at the time of the study, were not utilized. What fraction this group comprises of the entire body of patients referred to the Cancer Institute for purely palliative or custodial care cannot, unfortunately, be determined. However, in our overall estimation, 70 per cent of the patients admitted are definitely benefited by palliative methods of treatment and some 5 per cent of advanced cancer patients may be considered as salvaged. This compares not unfavorably with an approximate five-year cure rate of 18 per cent generally reported for all cancers.

With only three exceptions all patients received secondary radiation, radium, or radon therapy, usually in several cycles. The techniques used varied considerably, in view of the variety of neoplasms treated, and are therefore not detailed, but total amounts comprised adequate accepted tumor lethal doses in all instances. The series is constituted as follows: nine advanced re-

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TABLE I—CONT'D

COMPLICATIONS	PRIOR THERAPY	RADIATION AND RADIUM	SURGICAL PROCEDURES	"SALVAGED" YEARS ACTIVE SURVIVAL	STATUS
Intestinal obstruction, toxemia	Colostomy	--------	Radical colectomy	4	Cure
Colostomy; obstruction	Mikulicz type resection	Repeated courses	Secondary abdominal perineal resection	2½	Arrested
Postradiation, frozen pelvis	Perineal resection, radiation	Repeated courses	Secondary resection, colostomy	8	Arrested
Frozen pelvis, intestinal obstruction	Radiation	Repeated courses	Secondary radical excision and panhysterectomy	5	Cure(?)
Frozen pelvis, pyelonephritis, pathologic fracture hip	Radiation	Repeated courses	Repeated cystoscopic drainage, spica	6	Arrested
Frozen pelvis, pyelonephritis, pathologic fractures spine and hip	Radiation	Repeated courses	Orthopedic, cystoscopic, paravertebral injections	6	Arrested
Ulceration, infection	Radiation	Repeated courses	Repeated electrosurgical excisions	7	Cure
Pain, weakness	Radiation	Repeated courses	Orchiectomy (stilbestrol)	2½	Improved
Ulceration, infection	Radiation	Repeated courses	Radical excision of primary lesion and groin dissection	3	Arrested
Ulceration, infection	Local excision	Repeated courses	Radical resection of primary lesion, popliteal and inguinal glands; Schede operation for para-aortic glands	4	Arrested

current epitheliomas of face, oropharynx; and larynx, all extensive lesions with regional spread; one adamantinoma; one carcinoma of thyroid with local recurrence and pulmonary metastasis; one mixed tumor of salivary gland; one malignant lymphoma; four extremity tumors, namely a sarcoma, an epithelioma, a neurogenic sarcoma, and a melanosarcoma; three thoracic wall tumors, two neurogenic sarcomas, one osteochondrosarcoma; seven breast cancers, almost all with osseous metastases; two retroperitoneal tumors, one a neurocytoma, the other a hypernephroma; eight gastrointestinal carcinomas, two gastric, one jejunal, four colonic, one rectal; one of ovary, two of prostate. Two patients presented multiple lesions.

In all, sixteen were recurrences after primary excision had been attempted. Five had been laparotomized and considered inoperable, except for a palliative enterostomy. Primary resections were carried out in one-half the cases, most often by electrotherm cutting current in multiple stages for symptomatic relief by excision of extensive infected ulcerative or fungating lesions. In

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most of the remainder, radical secondary resection with hope of tumor extirpation was carried out. In several instances radiation alone sufficed. The operative procedures included carotid ligation, block dissection of neck, mandibular resection, laryngectomy, disarticulative amputation, radical inguinal and retroperitoneal dissection, gastrectomy, secondary enterectomy, abdominoperineal resection, panhysterectomy, and orchiectomy. There were six successfully treated pathologic fractures in the series, three of the spine and three of the hip, receiving a combination of orthopedic and radiologic treatment.

The average survival of four and one-half years is in each patient attributable to intensive and repeated roentgen therapy and surgical treatment, most often in combination. This assumption is borne out by the fact that such grave complications as intractable dysphagia, dyspnea, vomiting, pathologic hip or spine fracture, intestinal obstruction, hemorrhage, obstructive hydronephrosis and pyelonephritis, infection or toxemia had already supervened in most cases. In twenty-four patients presumptive cures and in nine instances definite arrest have been attained; the remainder are notably improved. The major features of each case are presented in some detail in Table I.

CONCLUSION

Both the variable neoplastic growth rates encountered and the incidence of prolonged periods of latency in cancer warrant considerable promise of prolonging life expectancy in many incurable patients with malignant disease. Significant arrest of the tumor process and appreciable augmentation of the comfortable longevity of the patient may in many instances be induced by the judicious administration of surgery, radiation therapy, and medication. On occasion a five-year survival with apparent cure may be achieved. The all too prevalent attitude that nothing can be done overlooks the remarkable progress in remedial therapy that has been accomplished. Proper management in the majority of primarily ineradicable malignancies may accomplish at least as much as in the present-day care of such similarly incurable illnesses as arteriosclerotic and rheumatic heart disease or hypertension and nephritis. Abandonment of the large group of patients with incurable cancer to uncontested early mortality after exploratory operation can only frustrate in large measure the campaign of public health education concerning prompt cooperation in cancer diagnosis and treatment. Forty-two patients with palliatively treated advanced cancer now surviving an average of four and one-half years are presented.

The fact that at present some four-fifths of all cancer patients are ultimately candidates for palliative treatment makes the exaction of the total potential life and comfort salvage in this group a public health problem of tremendous significance. The relief of pain and discomfort, the eradication of distressing primary and secondary lesions, the control of hemorrhage and infection, the recession of osseous metastases and healing of pathologic fractures, the successful management of dyspnea, dysphagia, and cough, and the postponement of regional and systemic spread of the primary neoplasm are among the desirable results achieved by the great armamentarium of modern palliative methods. In the province of advanced cancer this paraphrased dictum is truly applicable, "the physician can cure on occasion, help often, but provide comfort always."

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A REVIEW OF 101 SUBTOTAL GASTRECTOMIES FOR BENIGN ULCER

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THE 101 subtotal resections upon which this study is based have been performed during the past eleven years. It has been our policy to be neither the first nor the last in the adoption of an operation, and neither too conservative nor too radical in its practice. With added experience, however, it is but natural that our viewpoint has broadened and, in common with other surgeons, we have increased the scope of the procedure. We therefore feel that the findings, treatment, and results in these 101 cases are probably representative and may be of some value in an estimation of the indications, extent, and efficacy of resection of the stomach for benign gastric ulcer and for duodenal ulcer and its complications, according to modern conception.

GASTRIC ULCER

In selecting our patients with gastric ulcer for resection, we have always regarded chronic perforation, hemorrhage, obstruction, and associated extensive gastritis as definite criteria. Operation in such cases should be delayed only while the patient is being prepared, as these lesions are recalcitrant to medical treatment and continued conservative management is both useless and dangerous. In that more indefinite group, the uncomplicated ulcers, we have occasionally been somewhat less certain as to the proper course to pursue. Formerly, we were inclined to temporize with medical management unless malignancy seemed probable. Within recent years, we have taken a more aggressive course. We have appreciated more and more the fact that evidence of healing of a gastric ulcer after a period of medical treatment by no means signifies that the lesion is benign. By far the majority of carcinomas will also respond temporarily to medical measures. Not only this, but ulcer may be indistinguishable clinically from carcinoma. The usual ulcer symptoms in a comparatively young individual, associated with high stomach acids and a roentgenographic picture of a small lesion may also apply to carcinoma. In a study of our own cases of gastric cancer, we found that a preoperative diagnosis of ulcer was made in 22 per cent, and in a few others a distinction could not be made between ulcer and carcinoma prior to operation. Walters[7] reported that in 33 per cent of the cases of carcinoma of the stomach in which operation was performed at the Mayo Clinic over a period of thirty-two years, the characteristic symptoms of ulcer were described in the history. Further, Judd and Priestley[5] found that approximately 7 per cent of patients who have a resection for malignancies of the stomach are less than 40 years of age; approximately 9 of 10 carcinomas are 4 cm. or less in diameter; and a roentgenographic diagnosis of ulcer is made in approximately 10 per cent of carcinomas proved at operation. Again, the possibility of diagnostic error is forcefully demonstrated by Allen and Welch.[1] They report that of 69 patients subjected to gastric resection with a preoperative diagnosis of ulcer, 30, or 43 per cent, had a final diagnosis of cancer by the pathologist. Further, of 175 patients treated medically for ulcer, 13 were

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eventually found to have cancer. They regard this as an illustration of the difficulty of making a true diagnosis even while the lesion is under observation.

Nor is the *location* of the ulcer a definite indication of its benign or malignant nature. As a rule, lesions situated at the pylorus or in the antrum and on the greater curvature are malignant, whereas those in the mid-portion or proximal half and on the lesser curvature of the stomach are more often benign. Even in the latter areas, however, the potentiality of cancer is by no means negligible; at least one-third of the lesions so situated are malignant.

In so far as symptomatic relief is concerned, statistics indicate that medical treatment is curative in less than one-half the cases of gastric ulcer. Many patients must follow a medical regimen continuously for an indefinite period, and every one should have frequently repeated roentgenographic studies until cure is fairly certain. On the other hand, gastrectomy may be relied upon to relieve the symptoms completely or at least materially in almost 100 per cent of cases. Added to this, resection eliminates the danger of malignancy and practically eliminates the danger of a recurrent ulcer. In our experience, patients have obtained uniformly good stomach function, and thus far none has exhibited signs of a recurrent lesion.

The mortality of gastric resection in properly selected cases cannot well be held as an argument against its use. In the presence of an ulcer situated high on the lesser curvature, one must often compromise upon gastroenterostomy. The general condition of the patient may also prohibit resection. When the location of the ulcer permits and the patient is a suitable risk, the operation should be performed with a mortality of not over 5 per cent, which is only one-half the percentage of malignant degeneration.

Considering this fact and the fact that medical measures are curative in not more than 50 per cent of cases, whereas the prospect of permanent relief by resection is excellent, both medical and surgical opinion are tending more and more toward the latter procedure as the treatment of choice for uncomplicated gastric ulcer. Conservative management is reserved for those in an obviously early stage of development, preferably in the proximal portion of the stomach. If the symptomatic and roentgenographic signs disappear within three or four weeks, one may then feel that operation may be safely withheld so long as frequent checkup roentgenograms remain negative. Persistent or recurrent symptoms and signs after this brief period of medical treatment are regarded as definitely indicating surgery.

DUODENAL ULCER

The observer of trends in the treatment of duodenal ulcer cannot but be impressed with two facts: first, that although this lesion is now recognized as being an essentially medical disease, the number of patients who require surgery has not decreased. A review of our own cases over the past eleven years reveals that now approximately 33 per cent of patients with duodenal ulcer come to operation, whereas prior to this period approximately 30 per cent required surgery. Our criteria for operation having remained unchanged, we have no explanation for this other than that we are seeing more patients with surgical ulcers. Second, our conception of the choice of operation has been considerably altered. Acute perforations, constituting approximately 16 per cent of the duodenal ulcers we have seen which demand surgery, are usually treated by simple closure. Parenthetically, it is worthy of note that even in certain of these cases a few surgeons are now employing resection. Aside from this group, however, palliative surgery has to a large extent been replaced by

resection. Pyloroplasty has been abandoned almost entirely, and gastroenterostomy is employed by most surgeons only when the condition of the patient precludes the more radical operation, or when the lesion is situated so far distally on the duodenum as to encroach upon the common duct. We have not performed a pyloroplasty in our clinic since 1939, and in that year performed only one. In 1940, resection was done in one-half of our patients with primary duodenal ulcer, and gastroenterostomy in the other half; today three-fourths are treated by resection. Other clinics report a similar experience. Walters and his associates[8] reported that in 1940 gastroenterostomy constituted 55 per cent of operations for duodenal ulcer at the Mayo Clinic, and gastrectomy a little over 40 per cent. In 1942, this was reversed; gastrectomy was performed in over 57 per cent, while gastroenterostomies fell to approximately 41 per cent. Marshall[6] reported that at the Lahey Clinic during the past seven years, 395 patients were operated upon for peptic ulcer, aside from those with acute perforation. Of this 395, subtotal resection was performed in 318 and gastroenterostomy in 75 cases. Hinton[4] stated that he has performed subtotal gastric resection exclusively in his cases of chronic gastric and duodenal ulcer since 1932. All this means that surgeons have become convinced of the superiority of resection over gastroenterostomy when such a course is feasible. Further, one cannot overlook the fact that improved methods of preoperative treatment have made the procedure feasible in an increasing number of cases.

It has been our custom to advise resection in the presence of one or more of the following complications: (1) recurrent hemorrhage, (2) obstruction, (3) intractable pain, and (4) recurrent or reactivated ulcer.

Hemorrhage.—Primary resection has been performed for repeated episodes of bleeding in one-third of our surgical cases. Operation has been limited to those patients in whom the hemorrhage recurs often and is associated with long-standing symptoms of ulcer, particularly *pain.* On exploration, an ulcer is usually found on the posterior duodenal wall, its base extending deep into the pancreas. As a rule, the bleeding is produced by erosion of one of the larger pyloric group of vessels. The pain is generally due to edema and obstruction incident to a more or less severe inflammatory reaction of the pancreas, as well as to acid corrosion of the ulcer and pylorospasm. Not infrequently, an anterior ulcer is likewise present, and occasionally one encounters an anterior ulcer which itself is hemorrhagic.

If the hemorrhage is of massive proportions, there may be some question as to the advisability of operating immediately or delaying the procedure. In young individuals, that is, under 45 years of age, we feel that operation is indicated only if transfusions and other supportive treatment fail to control the bleeding and raise the blood pressure to a satisfactory level within thirty-six to forty-eight hours. With few exceptions, a clot will form and close the opening of the bleeding vessel in this group of patients. Not infrequently, the hemorrhage is the first evidence of ulcer and the patient has had no opportunity to try medical treatment. If the ulcer is of long standing, however, and medical treatment has been given an adequate trial, we believe resection is advisable as soon as the patient sufficiently recovers. In any event, a second massive hemorrhage is a definite indication for operation. A single massive hemorrhage in patients beyond the age of 45 is more serious. The arterial walls are less elastic and the formation of a clot is less likely. In this group it is best to operate within twelve to twenty-four hours unless continuous or repeated transfusion brings about a definite improvement; even so, operation should be per-

formed as soon as feasible following cessation of the hemorrhage. We have had only a few patients whose hemorrhage could be classified as massive, all of whom have recovered. Reports of large series, however, have shown that operation for massive hemorrhage in individuals over 45 years of age carries a high mortality, especially if the procedure is delayed beyond the first twenty-four hours after onset.

Obstruction arising from inflammatory edema of an otherwise uncomplicated ulcer may generally be overcome by medical treatment. On the other hand, in the presence of edema associated with a penetrating posterior lesion combined with a cicatrizing anterior ulcer, resection becomes necessary; medical treatment is advisable only as a preoperative measure, or the obstruction may be of such long standing as to have produced an enormous dilatation of the stomach and to be entirely unresponsive to conservative management. In these cases, we believe resection affords the only promise of relief. We have recently encountered a lesion of the latter type in a woman, aged 36 years. She had had attacks of abdominal pain for as long as she could remember, and definite ulcer symptoms for fifteen years. During recent years she had vomited daily. Having undergone many examinations and much treatment, with no relief, she was referred to us for surgery. Our examination revealed, in addition to the obstructing duodenal lesion, an enormous stomach, the greater curvature lying on the pelvic floor when the patient was in the standing position. These findings were confirmed at operation. An anterior ulcer, which had slowly perforated and was being protected, was producing an almost complete obstruction. The stomach was twenty inches or more in length and of commensurate depth, its walls exceedingly edematous. A subtotal resection was followed by prompt relief of symptoms.

In this connection, the presence of an anterior ulcer should always lead one to suspect a posterior lesion as well, whether indicated by the symptoms or not. It is now well known that the majority of ulcers are multiple, and unless a careful search is made a posterior lesion may go undetected. Frequently, it is necessary to open the stomach to bring the latter into view. We have encountered multiple lesions in 62.5 per cent of the primary resections we have done for ulcer.

A small number of patients with ulcer, usually those past middle age with a history of constant or recurrent symptoms covering many years, require operation because of mechanical obstruction at the pylorus incident to the long-standing inflammation and consequent cicatrization. Formerly, this was the one complication for which gastroenterostomy was considered ideal. Experience has shown that it is the one most amenable to cure by gastroenterostomy; the stomach acids are practically always low and the result generally excellent. Nevertheless, within the past two years we have been performing resection in this group of patients, also, as the procedure of choice. There are several reasons for this change of attitude. In the first place, the stomach is considerably enlarged and the small gastroenterostomy opening does not permit the contents to empty quickly enough. Second, the patient has a much quieter and more rapid convalescence. Third, the technical procedure is more easily executed, there being no firm adhesions between the duodenum and pancreas. Fourth, by removal of the ulcer-bearing portion of the stomach we have every assurance that we have permanently rid the patient of his disease. Although the likelihood of recurrence following gastroenterostomy in these cases is remote, it is certainly worth considering.

Intractable pain, which is practically always accompanied by high acid values and the digestive symptoms of ulcer, is our major reason for resection in a large proportion of cases. Realizing the difficulty of relieving these patients by any type of treatment, we have attempted to select them with care. Operation has been advised only after prolonged medical treatment has proved ineffectual or if the patient has shown himself incapable of following a medical regimen for occupational or other reasons. On exploration, one usually finds both an anterior and a posterior ulcer, the latter penetrating into the pancreas and being chiefly responsible for the persistent symptoms. After operation, it is often necessary to observe the patient at brief intervals for an indefinite time. This is especially true of those of unstable temperament, since such individuals will frequently continue to complain, despite every physical and roentgenographic appearance of an excellent result.

Gastrojejunal ulcers are observed most often in young or middle-aged individuals with high acid values who have had a gastroenterostomy. Many of them appear within a few days or a few weeks following operation, and the majority manifest themselves within eighteen months. Although years may elapse before the patient comes to surgery, the history will usually reveal that the symptoms recurred within a short while after operation. The symptoms, however, are not quite typical: the pain is slightly lower and more to the left, is more constant and severe, and is seldom completely controlled by food or alkali. Bleeding, often serious, has been associated in one-third of our cases.

According to our observation, medical treatment for these ulcers gives only temporary relief. For this reason, we regard operation as imperative as soon as the patient can be prepared. Perforation into the peritoneal cavity, and especially into the transverse colon, is always a possibility. Frequently, also, the necessity for operation is increased by the presence of an active duodenal ulcer. During the past eleven years we have operated upon eight patients for gastrojejunal ulcer, all except one of whom had an associated duodenal ulcer. One patient had not only a duodenal ulcer, but two gastrojejunal ulcers, one penetrating into the pancreas and one into the colon. In 3 of the 8 cases the gastrojejunal ulcer had penetrated onto the transverse colon, and in an additional 2, or 25 per cent, a gastrojejunocolic fistula was present.

Extent of Operation.—Experience has shown that the ultimate success of gastric resection depends chiefly upon its extent. The object of the operation is the control of hypermotility and hypersecretion and, by this means, relief of the patient's symptoms. It is now well known that the major factor in recurrent ulcer following resection is failure to remove the pylorus and antrum, this being the portion which is largely responsible for activity of the acid-bearing cells. Thus, the operation should invariably be one which completely extirpates the antrum, pylorus, and ulcer. If such a procedure is not technically feasible because of extensive ulceration or inflammatory reaction, it is better to be content with a gastroenterostomy; if necessary, an adequate resection may be performed after a period of physiologic rest.

Follow-up studies have proved that, with few exceptions, 55 to 65 per cent of the distal portion of the stomach, together with the ulcer, is ample to fulfill all the requirements of resection for primary duodenal ulcer. Some surgeons, however, consider it advisable to resect three-fourths or more, contending that absolute achlorhydria is essential to prevent recurrence. With this we cannot agree. The disturbance of gastric function and the total anacidity incident to such wide resections may lead to serious nutritional deficiencies. Friedell,

Sharr, and Walters[3] found that when one-half or more of the stomach, including the pylorus and antrum, is removed, a permanent reduction of the free hydrochloric acid in the fasting contents follows, and this reduction is to 0 in 75 per cent of cases. If more than this amount is removed, there is only a slight increase of the incidence of the reduction to 0. The remaining 25 per cent does not obtain relative achlorhydria, even though the entire pylorus is resected. It seems quite likely, as they suggest, that marginal ulcers following resection develop in the 25 per cent; unquestionably, those who are not completely relieved are in this group. Church and Hinton[2] reported that 46 per cent of their patients had no free hydrochloric acid postoperatively, including not only those who were regarded as cured, but also a number who were merely benefited and even unimproved. We have found that a relative achlorhydria gives excellent results and see no point in depriving the patient of any more of the stomach than is necessary. In fact, it is our conviction that removal of 50 per cent for primary duodenal ulcer in a patient with low acids is just as effective as the more massive resection, and that excision of more than two-thirds is unwarranted unless the acids are excessive or an extensive gastritis is present. A recurrent or marginal ulcer, of course, demands a higher resection. These patients are unlikely to be relieved entirely by any method of treatment, though we may reasonably promise them a comparatively comfortable existence by removal of 75 to 80 per cent of the stomach. Even so, medical treatment for an indefinite period after operation is often advisable.

The Polya type of anastomosis is employed routinely in all our gastrectomies. Formerly, an effort was made to reconstruct the continuity of the intestinal tract posterior to the colon in every case. More recently, however, we have been using the antecolic anastomosis, as suggested by Balfour, in an increasing number. With these techniques, we believe the acid factor is better controlled by reason of the rapid emptying, which limits the admixture of acid with the stomach contents, and by reason of the fact that the maximum amount of bile is admitted into the stomach through the larger opening. During the early postoperative period, too rapid emptying is prevented by spastic contracture of the jejunum, and after healing is complete the jejunum acquires a certain immunity to the stomach acids and itself assumes some degree of digestive function. In addition to these features, obstruction incident to adhesions or to contracture of the stoma from scar tissue is less likely following the Polya anastomosis.

We have never performed an additional enteroenterostomy, even in our highest resections for ulcer. This procedure is not only unnecessary, but tends to prevent a material reduction in gastric acidity and thus increases the danger of recurrence.

ANALYSIS OF CASES

In making this study, we have reviewed all our cases of gastric, duodenal, and gastrojejunal ulcer over the past twenty-six years, comprising a total of 1,218. Of this number, 1,147 (94.2 per cent) were duodenal, 45 (3.7 per cent) were gastric, including 8 in which both a gastric and duodenal ulcer were present, and 26 (2.1 per cent) were gastrojejunal. These figures, together with the number of each type in which operation was performed, are shown in Table I.

As may be seen, in our experience the incidence of gastric ulcer has been quite low in proportion to the incidence reported by others, being 3.7 per cent

TABLE I. PATIENTS WITH ULCER, JANUARY, 1918 TO JANUARY, 1944 (1,218)

	PATIENTS	OPERATIONS	PER CENT
Duodenal ulcer	1,147	350	30
Gastric ulcer (8 duodenal ulcer)	45	27	60
Gastrojejunal ulcer	26	16	60
Totals	1,218	393	32.4

of the entire 1,218, or 1 in every 27. Further, the gastric ulcers for which operation was done were only 7 per cent of the total of 393 surgical ulcers. We have no explanation for this, as we have been most careful to locate every ulcer definitely and to record its location.

For purposes of comparison, the series of 1,218 ulcers has been divided into two groups: those observed prior to January, 1933, when we first began the use of gastrectomy for duodenal ulcer, and those from 1933 to 1944. The distribution of the ulcers and the operations performed are shown in Tables II and III.

TABLE II. PATIENTS WITH ULCER, 1918 TO 1932, INCLUSIVE (600)

	PATIENTS	OPERATIONS	PER CENT
Duodenal ulcer	564	167	30
Gastric ulcer (2 duodenal ulcer)	24	12	50
Gastrojejunal ulcer	12	8	66
Totals	600	187	30.1

TABLE III. PATIENTS WITH ULCER, JANUARY, 1933 TO JANUARY, 1944, INCLUSIVE (618)

	PATIENTS	OPERATIONS	PER CENT
Duodenal ulcer	583	183	31
Gastric ulcer (6 duodenal ulcer)	21	15	71
Gastrojejunal ulcer	14	8	57
Totals	618	206	33.4

The cases in these two series are similar in type and number, though the percentage of total operations is slightly higher in the latter group. This holds true even when one omits the operations for acute perforating ulcer, which in the first group is 27 per cent and in the second group, 28 per cent. The types of operations employed in the two groups of cases are shown in Table IV.

TABLE IV. TOTAL OPERATIONS IN 1,218 PATIENTS WITH ULCER, 1918 TO 1944

	CLOSURE PERFORATION	PYLOROPLASTY	GASTROENTEROSTOMY	RESECTION	TOTAL
Group I					
600 cases 1918-1932	24	35	125	3	187
Group II					
618 cases 1933-1944	33	14	58	101	206
Totals	57	49	183	104	393

These figures clearly show our trend toward resection as the procedure of choice for ulcer during recent years. Of the 3 cases for which resection was done in the earlier group, 2 were for gastrojejunal ulcer and 1 for gastric and duodenal ulcer combined. The lesions for which resection was done in the second group are shown in Table V, together with the mortality.

In 2 cases of gastric ulcer the lesion was so high as to preclude resection and a gastroenterostomy was necessary.

In the 61 operations for primary duodenal ulcer and the 6 for duodenal and gastric ulcer combined, a total of 67, there were 42, or 62.5 per cent, multiple ulcers.

TABLE V. FINDINGS AND MORTALITY IN 101 RESECTIONS FOR ULCER, JANUARY, 1933 TO JANUARY, 1944

	NUMBER	MORTALITY	PER CENT
Primary Operations			
Duodenal ulcer	61	1	1.7
Duodenal and gastric ulcer	5	0	0
Gastric ulcer	7	1	14.3
Totals	73	2	2.7
Secondary Operations			
Duodenal ulcer	19	0	0
Duodenal and gastric ulcer	1	0	0
Gastrojejunal ulcer	6	0	0
Gastrojejunal ulcer with colon fistula	2	1	50
Totals	28	1	3.6
	101	3	3.0

On studying these 101 patients with regard to the *results* of resection, we find that of the 13 patients with gastric ulcer, including those with duodenal ulcer as well, 11 were operated upon from nine months to nine years ago. Of these 11 patients, 10, or 90 per cent, obtained a good functional result and were free of their former ulcer symptoms. The eleventh patient died of a pulmonary embolism on the third postoperative day.

Of the 61 patients with primary duodenal ulcer, 1, or 1.7 per cent, succumbed to pneumonia postoperatively. This, incidentally, was the first patient of the series, operated upon in 1933. Of the remaining 60, 50 were operated upon more than one year ago. Two of these 50 have not been heard from since leaving the hospital. Of the other 48, 33 report an excellent result, with good stomach function and complete relief of their distress. An additional 10 have been materially relieved, though they still have some minor disturbance, such as mild nausea and vomiting after breakfast, or some weakness or stubborn weight loss. These 43 patients represent 90 per cent of results which may be classified as excellent or good. Four patients, or approximately 8 per cent, have clinical and roentgenographic evidence of a recurrent ulcer at the stoma.

The total operative mortality of the 73 patients operated upon primarily was 2, or 2.7 per cent. Of the 28 for whom resection was performed as a secondary procedure, 1 died, this being a mortality of 3.6 per cent. The latter patient was one of the two who had a gastrojejunocolic fistula. The fistula had been present for six months. Death was due to pneumonia.

It is of interest to study these results of resection for primary duodenal ulcer from the standpoint of the pathologic condition found at operation, as shown in Table VI.

TABLE VI. RESULTS OF GASTRIC RESECTION IN FORTY-NINE CASES OF PRIMARY DUODENAL ULCER

	COMPLETE RELIEF	PARTIAL RELIEF	NO RELIEF	DIED	TOTAL	PER CENT
Bleeding ulcer (7 multiple)	13	4	0	0	17	34.7
Obstructive ulcer (2 multiple)	5	1	0	0	6	12.2
Intractable ulcer (16 multiple)	15	5	5	1	26	53
Totals	33	10	5	1	49	100

It will be seen that 17, or 34.7 per cent, of the patients who were operated upon more than one year ago had a bleeding posterior ulcer, 7 of them with an associated anterior ulcer. Thirteen of the 17 were completely relieved and 4 partially relieved. Thus, the entire 17, or 100 per cent, were benefited by the operation. There were no deaths in this group.

Five of the 6 patients with obstructive ulcers have remained entirely free of symptoms, and 1 still has some nausea with vomiting of bile at times. Two of the 6 had both an anterior and a posterior lesion.

Of the 26 for whom resection was performed for intractable pain, 15 were completely relieved, 5 partially relieved, 4 continued to have considerable discomfort, 1 developed clinical evidence of a gastrojejunal ulcer, and 1 died. Sixteen of the 26 had multiple ulcers.

Although this series is small, it shows that our experience is similar to that of other surgeons, in that obstructive ulcers of the duodenum have been found most amenable to cure, that resection for bleeding ulcer may be expected to give the next best results, and that for intractable ulcers the prospect of complete relief is somewhat less certain.

Of the total of 8 patients for whom resection was performed for gastrojejunal ulcer, all were operated upon more than one year ago. Six have obtained an excellent result, having no symptoms whatever, and 1 has only occasional nausea. These 7 constitue 87.5 per cent of good results. The remaining patient, who had a gastrojejunocolic fistula as mentioned previously, died, constituting a mortality of 12.5 per cent in the group of 8.

Of the other 19 patients who had resection following a previous operation, 16 came to surgery more than one year ago. Three of these have some slight nausea, and the others report complete relief with a good functional result.

TABLE VII. MORTALITY OF 101 PATIENTS WITH RESECTIONS OF THE STOMACH FOR BENIGN ULCER

	NUMBER CASES	NUMBER DEATHS
Primary duodenal ulcer	61	1
Gastric ulcer (6 with duodenal ulcer)	13	1
Gastrojejunal ulcer	8	1
Reactivated duodenal ulcer	19	0
Totals	101	3 (3%)

In Table VII is presented a composite picture of our mortality of resection for all types of benign ulcer of the stomach and duodenum. In a total of 101 resections, we have had 3 deaths, a mortality of approximately 3 per cent. Considering the nature of the operation and the fact that many patients with these lesions have associated disease which materially increases the risk, we feel that a mortality of 5 per cent or less is certainly commensurate with that of other abdominal procedures of similar magnitude. We have had no deaths from resection in these cases for the past eight and one-half years.

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DICUMAROL IN THE PREVENTION OF POSTOPERATIVE THROMBOSIS AND PULMONARY EMBOLISM

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AT THE time of John Hunter and Cruvelhier, pathologists were of the opinion that thrombosis occurred as a sequel to phlebitis. In 1846, Virchow[1, 2] began his experimental work on thrombosis and during the next ten years completely revolutionized all existing knowledge on this subject. He demonstrated conclusively that a thrombus is the primary essential condition in phlebitis. He was also the first to recognize pulmonary embolism. This work was his single greatest achievement in pathology and is in every sense his very own.

Postoperative thrombosis and pulmonary embolism have always been a source of great concern to the surgeon. A successful operation coupled with an uneventful subsequent convalescence does in no way guard the patient against a possible fatal embolism.

In a review of the literature[3-5] we find that the incidence of venous thrombosis and pulmonary embolism is 1 per cent of all surgical procedures, 2 per cent of all laparotomies, and 3 per cent of laparotomies performed on women. The occurrence after splenectomy is as high as 5 per cent. Since the platelets are very much increased after the operation this is undoubtedly a contributing factor.

Infection and extensive resection of tissue increase the occurrence of thrombosis and embolism. Other predisposing factors according to Barker and his co-workers are obesity, blood diseases, heart disease, peripheral vascular disease, and malignancy.

Many factors are involved in the production of postoperative venous thrombosis, the most important of which are local changes in the wall of the veins, the rate of venous flow, and disturbances in the coagulation of the blood. According to Neumann[6] and Voegt,[7] thrombophlebitis begins in the pelvic venous plexuses where complete stasis is possible or in the venules of the subcutis and muscles of the calves and thighs where prolonged pressure and ischemia cause tissue damage. Complete postoperative bed rest predisposes to lesions in the legs.

Thrombophlebitis rarely occurs in the first four days after operation. It makes its appearance between the fourth and the fourteenth day. Pulmonary embolism, on the other hand, is more often seen between the seventh and the fourteenth postoperative day. When thrombophlebitis does occur, postoperatively, it generally involves the veins of the lower extremities or, if intra-abdominal, the veins of the pelvis. The veins of the left leg are involved twice as frequently as those of the right, the short saphenous being the most commonly affected. Nevertheless, this condition can occur in any of the veins. The

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thrombus may either adhere to the wall of the vein and become organized, or it may detach itself to form an embolus. The degree of pulmonary involvement depends upon the size of the embolus. An embolus arising from the saphenous vein would be relatively harmless, while one from the iliofemoral would be of sufficient size to cause death. After a thrombophlebitis has existed a few days it is less likely to be a source of embolism, for the thrombus has become adherent to the wall of the vein. Most of the cases of pulmonary embolism arise from so-called silent thrombophlebitis which cannot be diagnosed. Even at autopsy in cases of fatal pulmonary embolus it is often impossible to find the etiologic thrombophlebitis.

Post-mortem studies have shown that many patients suffered from repeated small pulmonary emboli until one was of sufficient size to be fatal. This emphasizes the importance of prompt treatment in cases of small multiple emboli.

Until recently there was no effective treatment for postoperative thrombosis and pulmonary embolism. Some surgeons[8, 9] hoped to prevent this condition by having the patient get out of bed a day or two after the operation. The purpose of this was to improve the circulation in the lower extremities. Other less drastic physical measures recommended were turning the patient frequently to elevate the lower extremities and to exercise them. It was also advised to have patients breathe deeply and cough in order to keep the lungs clear and well aerated. Newer methods include paravertebral procaine sympathetic block[10] and venous section and ligation.[11]

In 1924, Mason[12] reported on the use of heparin in the prevention of thrombosis and embolism. This heparin was too toxic for general use. Ten years later Charles and Scott[13] and Murray and Best[14] in Toronto investigated its possibilities and found it effective in the treatment of thrombotic conditions. The use of heparin has many disadvantages: it is expensive, must be given intravenously, and is difficult to control.

In 1941,[15] with the synthesis of dicumarol, the answer to the treatment of venous thrombosis and pulmonary embolism seemed to have been found. Here was an agent that could be produced inexpensively in large quantities and which was effective orally. It changed the coagulation of the blood in the desired way and was easy to control if used intelligently.

Butsch and Stewart[16] tried dicumarol on a small group of patients with no untoward results. They started it forty-eight hours preoperatively so that the patient's prothrombin time was prolonged during and after the operation. No thrombosis occurred in this series. Barker, Allen, and Waugh[17] reported good results while using dicumarol. There was slight bleeding in 4 per cent of their patients postoperatively.

Shapiro and Sherwin[18] and Zucker[19] have also reported favorably on the safety of this drug. On the other hand there has been some adverse comment on the use of anticoagulant in the treatment of thrombophlebitis. The main criticism according to DeBakey has been that the series of investigations is not adequate, nor are the results sufficiently impressive to justify definite statements.

In an effort to evaluate the further use of dicumarol, we subjected a series of surgical patients to a prophylactic course of the drug. At the same time we used this drug in the treatment of cases of venous thrombosis and pulmonary embolism which arose on the surgical services. This experiment extended

from October, 1943, to July, 1944. The technique of administering the dicumarol and the method of performing the prothrombin test to control its use are of such paramount importance that they will be described in detail in the following paragraphs.

METHOD OF ADMINISTRATION

The simplest expression for the coagulation of blood in vitro based on the pioneer work of Morawitz, Fuld and Spiro is:

I. Prothrombin + Ca + thromboplastin = thrombin
II. Fibrinogen + thrombin = fibrin (clot)

Dicumarol acts by inhibiting the production of prothrombin at its source, namely, the liver.

Dicumarol is a tasteless, odorless white powder which is put up in 100 and 50 mg. capsules. A prothrombin determination is done before administration to find the patient's normal blood level. After this has been established 300 mg. are given. On the following day a prothrombin level is done again, and unless it is markedly prolonged 200 mg. are given. The object is to prolong the prothrombin time to twice its normal value. In other words, if normal is 17 to 20 seconds the therapeutic range would be about 34 to 40 seconds. It is desirable to keep the patient in this range during treatment. Naturally, every person reacts differently to drugs and it is necessary to adjust subsequent doses individually. In many cases the prothrombin time is prolonged rapidly and the prothrombin determination on the third day shows that the patient is in the therapeutic range. Then it is best not to give any drug on that day and see what the prothrombin level is on the fourth day. If still in the therapeutic range, no drug is given on that day either. On the other hand, if the prothrombin time is rapidly becoming shorter and the patients are getting out of the therapeutic range, 100 mg. of dicumarol are given. Other patients will be found who do not reach the therapeutic range with the first 300 and 200 mg. In these cases another 100 mg. are given on the third day and prothrombin observation made daily after that. The important thing in giving the drug is to remember that its effect is delayed and cumulative. It is better to proceed cautiously and give smaller doses than to plunge recklessly ahead. The essential principle, therefore, is not to give any dicumarol until after the prothrombin level has been recorded. When this has been done, given conservative doses, 100 mg. usually after the second day and never more than 200 mg. at a time, sometimes even 50 mg. is enough.

If bleeding should occur, a transfusion of fresh citrated blood plus 60 mg. of water-soluble vitamin K intravenously will raise the prothrombin level promptly.

Salicylates, notably aspirin, should not be given at the same time that dicumarol is being used. The reason for this is that dicumarol can be synthesized from salicylic acid and while the salicylates are only one-twentieth as active anticoagulants as dicumarol, they might produce an unforeseen intensified action if given together.

TECHNIQUE

Thromboplastin.—Rabbit's lungs.

Preparation:

1. Remove lung from freshly killed rabbit (A.Z. rabbits can be used to save expense).

2. Wash lung, to remove blood, for about fifteen minutes in cold running water; blot out excess with filter paper.
3. Cut in small pieces and place in evaporating dish.
4. Place dish in desiccator (drying agent BaO_2); attach to suction apparatus to form a vacuum.
5. Place desiccator in incubator at 37° C. for twenty-four hours (drying process).
6. Remove pieces of lung from desiccator, grind finely in mortar.

Thromboplastin.—

1. Rabbit's lungs (thrombo), 100 mg.
2. Add 5 c.c. of normal physiologic saline solution (0.85 per cent).
3. Inactivate for ten minutes in water bath at 57° C.; stir constantly.
4. Remove from water bath, stirring until thrombo reaches room temperature.
5. Add 5 c.c. of $CaCl_2$ (1.11 gr. to 500 c.c. H_2O); shake thoroughly.
6. Centrifuge for four minutes at 1,800 revolutions; use supernatant fluid.

Obtaining Blood Specimen.—

1. Use 4.5 c.c. of blood to 0.5 sodium oxalate; 1.34 gr. to 100 c.c. H_2O.
2. Centrifuge and remove plasma.

Prothrombin Determination.—

1. Place plasma in water bath kept at a constant 38° C. temperature.
2. In small tubes add 0.2 c.c. of thromboplastin.
3. To thromboplastin add 0.1 c.c. of plasma. Start stop watch immediately, using loop to determine when complete clot is formed; record time of result.

   Proper prothrombin determination is very important as the entire success of the administration of dicumarol depends upon the accuracy of the technique. The Wisconsin Research Foundation specifically recommends the use of rabbit's lung instead of rabbit's brain in the preparation of thromboplastin. The activity of the thromboplastin preparation should always be tested on control blood before the daily prothrombin determination is done.

DISCUSSION

From the experimental data, Table I, it can be seen that we treated 102 surgical patients prophylactically with dicumarol in an effort to prevent postoperative thrombosis and pulmonary embolus. Since the statistics show that this condition does not begin until approximately the sixth or seventh postoperative day, it was thought best to start the drug on the third to the fourth

TABLE I. PROPHYLACTIC CASES

DIAGNOSIS	NUMBER OF CASES	AVERAGE TOTAL MG. DICUMAROL	AVERAGE NUMBER OF DAYS IN THERAPEUTIC RANGE
Hernioplasty	37	800	5
Hysterectomy	19	700	6
Appendectomy	21	700	5
Cholecystectomy	3	700	4
Laparotomy	5	700	8
Miscellaneous	17	700	6

postoperative day. In this way the prothrombin time was not prolonged at the time of operation, and a few days were permitted to elapse postoperatively in order that healing might begin. That this time, namely the third or fourth postoperative day, was the most opportune day to administer the drug is shown by the fact that we found neither thrombotic phenomena nor postoperative bleeding.

Tables II and III illustrate the typical cases of venous thrombosis and pulmonary embolism that occurred after 2,591 general surgical and obstetrical procedures carried out during this experimental period. Dicumarol carefully administered in these cases resulted in uniformly favorable results. The thrombophlebitis cleared up promptly and none of the pulmonary emboli caused fatal results.

TABLE II. VENOUS THROMBOSIS

DIAGNOSIS	NUMBER OF CASES	AVERAGE TOTAL MG. DICUMAROL	AVERAGE NUMBER OF DAYS IN THERAPEUTIC RANGE
Hysterectomy	10	840	9
Postpartum	11	900	10
Hernia	3	850	10
Appendectomy	2	700	10
Gastric resection	1	600	12
Cholecystectomy	1	1,400	22
Lobectomy	2	600	8
Fracture of femur	1	1,400	23
Excision of tumor of leg	1	1,000	19
Amputation of leg (diabetic)	1	1,300	25

This latter observation is essentially important as it is well known that 20 per cent of the minor emboli result in death. Extreme care was again observed in the administration and control of dicumarol; consequently, there were no complicating hemorrhages. In acute pulmonary embolism it is proper to administer heparin by vein and start dicumarol by mouth at the same time. This should be done because dicumarol has a twenty-four to forty-eight hours' latent period and it is important to have the coagulation mechanism altered by the heparin until dicumarol takes effect.

TABLE III. PULMONARY EMBOLISM

DIAGNOSIS	NUMBER OF CASES	AVERAGE TOTAL MG. DICUMAROL	AVERAGE NUMBER OF DAYS IN THERAPEUTIC RANGE
Hysterectomy	4	1,090	15
Oophorectomy	1	1,800	17
Hernia	2	1,700	17
Amputation of leg	1	2,100	13
Saphenous ligation	1	1,400	13

Heparin is put up in 10 c.c. vials. One vial is mixed with a 500 c.c. saline infusion and given intravenously at the rate of 20 drops per minute. The blood coagulation time is done every four hours by the tube method. The purpose of the heparin is to prolong the coagulation to three times its normal figure. If normal is five minutes it should be kept at fifteen minutes. This is regulated by increasing or decreasing the rate of flow of the heparin. When the infusion bottle is emptied it is refilled with the same mixture, and this proce-

dure is kept up as long as heparin is needed. When the dicumarol administration is considered to be effective, heparin is stopped.

From our experience we feel that dicumarol is a safe means for preventing postoperative venous thrombosis and pulmonary embolism. Whether it should be used routinely is still a matter of debate. However, we are convinced that it should be given in all cases where thrombotic complications are likely to arise. This will include extensive pelvic operations, operation for abdominal malignancy, and operations on individuals who have previously shown tendency to thrombosis. Naturally, it is the drug of choice when these conditions have developed. From our experience we would further recommend that each hospital intending to use this drug should designate one member of its staff to familiarize himself with the methods of administration and laboratory control. This would guard against harm to the patient and injury to the reputation of an excellent drug.

CONCLUSION

1. Dicumarol is of definite value in the prevention of postoperative venous thrombosis and pulmonary embolism.

2. Dicumarol is the drug of choice in the treatment of thrombotic phenomena.

3. Dicumarol is a safe drug if administered intelligently after careful prothrombin determination.

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RETROGRADE ARTERIOGRAPHY IN THE STUDY OF THE ABDOMINAL AORTA AND ILIAC ARTERIES

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THE pathology of the abdominal aorta has received little attention from the clinicians due to the fact that there was no practical method for its exploration.

Plain radiographs may demonstrate calcification of the walls of the abdominal aorta or its branches, and may show the presence of aneurysms if their walls are calcified; but when calcification is not present or is very slight, plain x-ray investigation is of no practical value.

A method for the radiographic study of the abdominal circulation was described for the first time by Dos Santos in 1929. He proved the value of aortography in the study of a great number of pathologic conditions of the abdomen.*

The difficulty of the technique of the aortography described by Dos Santos requiring blind puncture of the aorta was a stumbling block in the generalization of this method which promised to be so valuable to the clinician. I tried to use Dos Santos' method of "blind aortography" in the course of experiments in the treatment of cancer of the abdominal organs with certain substances that became fluorescent when exposed to x-rays. To avoid the difficulties that arose with Dos Santos' method, I recommended the use of a new technique for the arteriographic study of the abdominal aorta which was presented at the forty-first meeting of the American Roentgen Ray Society, Boston, Mass.† This technique consists essentially in the puncture of the femoral artery at the level of Scarpa's triangle with a trocar through which a rubber catheter is introduced and passed into the iliac artery up to the desired level in the aorta. Through this catheter 25 to 30 c.c. of a 70 per cent solution of diodrast are injected at the rate of 5 c.c. per second. The trocar is then withdrawn, a stitch placed in the adventitia of the artery, and the wound closed. Using the same injection, urograms are taken after the aortography.

In view of the present difficulties to obtain rubber catheters, I was compelled to substitute the aortography by catheterization for the present "retrograde abdominal aortography." In this method the femoral artery is exposed by blunt dissection, under local anesthesia, at the level of Scarpa's triangle and punctured with a trocar 1.5 mm. in diameter. Through this trocar is injected 50 c.c. of a 70 per cent solution of diodrast in two and one-half to three seconds. Tourniquets must be placed at the roots of both lower extremities in order to avoid the passage of the contrast medium into the arteries of the legs. The Trendelenburg position may be required in certain cases. In experiments with dogs I was able to determine in the flouroscope that the opaque substance had to overcome first the inertia and then the blood pressure when it was injected. It reaches

This work was done at the Cancer Institute with the collaboration of Dr. P. Jimenez and Dr. Gomez Zaldivar.

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*Dos Santos, Reynaldo, Lanias, A. C., and Caldas, J. P.: Arteriography of the Extremities and of the Abdominal Aorta, Paris, 1931, Masson & Cie.

†Farinas, P. L.: Aortography by Catheterization, Am. J. Roentgenol. vol. 46.

a higher level during diastole and descends during systole, entering then into the branches of the abdominal aorta. To avoid changes in pressure when the opaque substance is injected by hand, I have designed an apparatus to maintain a constant pressure and rate of injection. It consists of a pump with a piston which acts upon the embolus of the syringe. The piston works by an air compressor with a regulator and a manometer (Fig. 1).

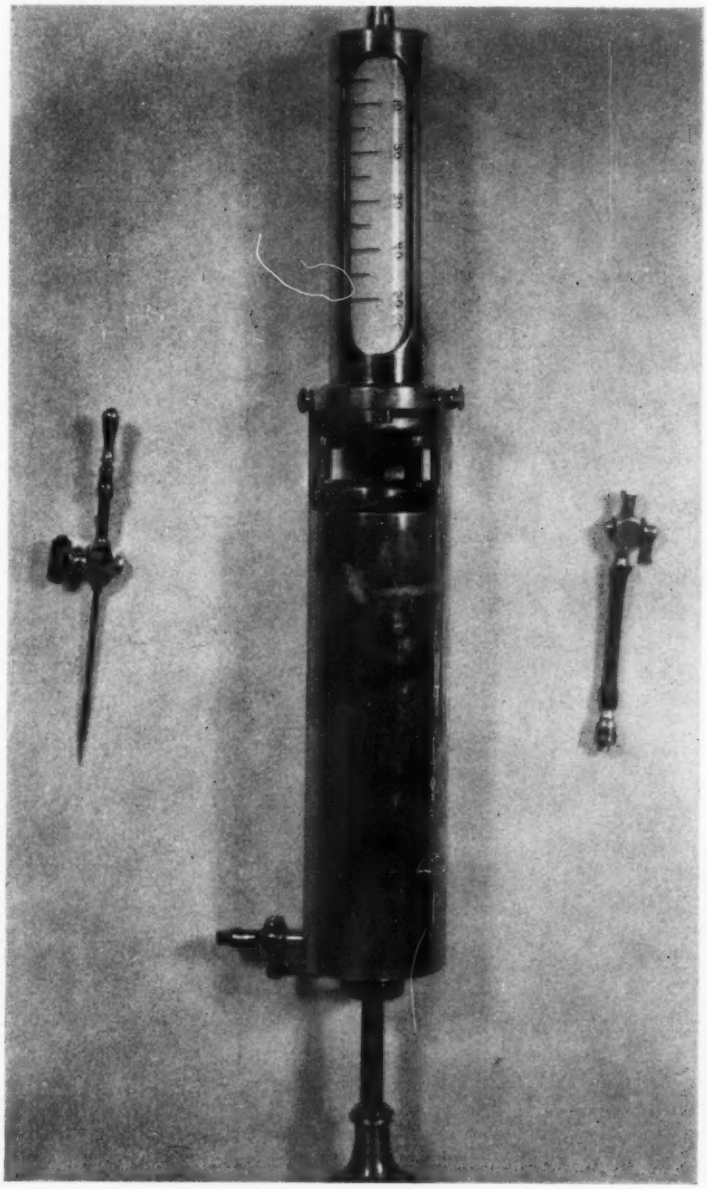

Fig. 1.—Instruments required: One trocar 1.5 mm. in diameter, one 50 c.c. syringe, a flexible rubber tube to connect the trocar to the syringe, a pump with a piston that acts upon the embolus of the syringe.

With a trocar 1.5 mm. in diameter and a constant pressure of fifteen pounds, it is possible to inject 25 c.c. of the opaque substance per second, the speed of injection being modified according to the blood pressure and the vascular condition of the patient. The first plate is taken when 40 c.c. of the opaque substance have been injected and a second immediately afterward, using a fast plate changer (Fig. 2.) When the injection is finished, the trocar

is withdrawn, a stitch placed in the adventitia of the artery at the site of the puncture, and the wound closed. The patient should be given a barbituric the night before, and morphine hypodermically one hour before the injection in order to obtain relaxation and avoid pain.

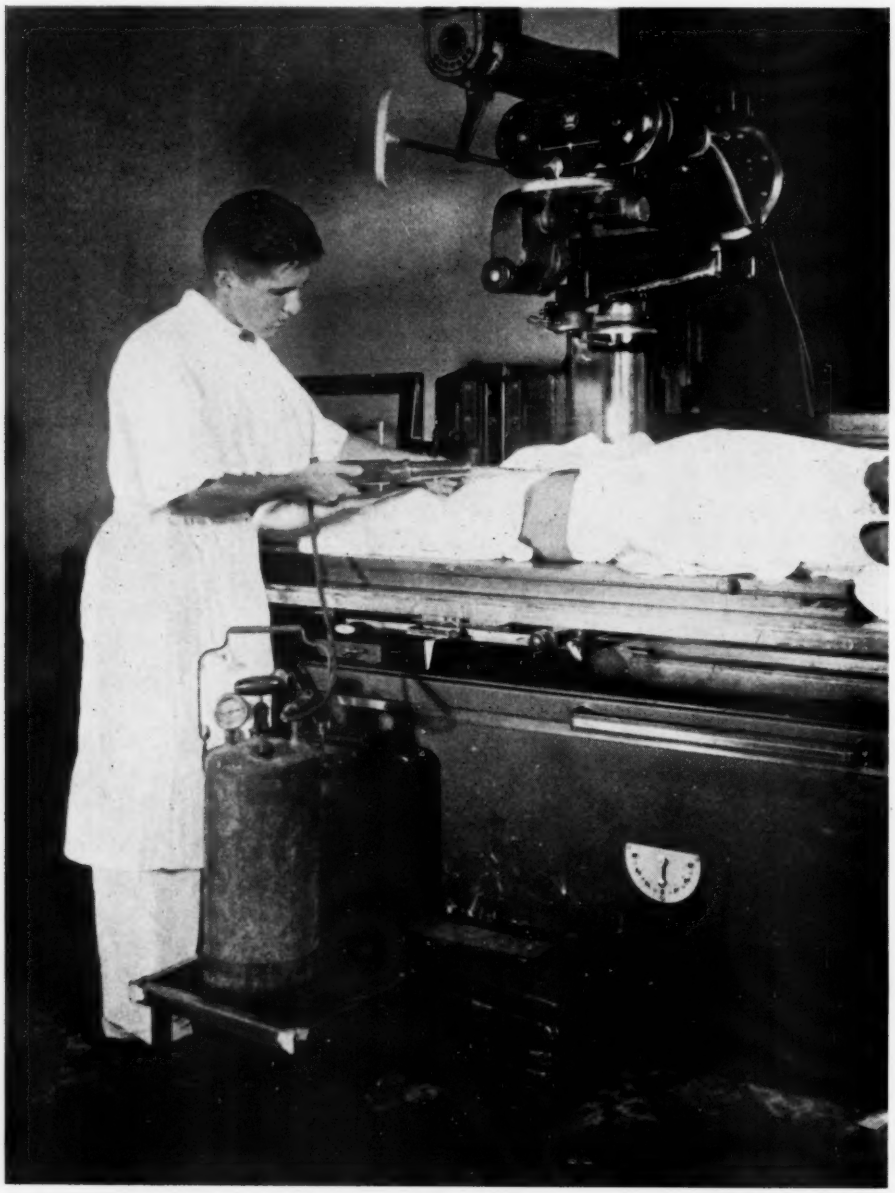

Fig. 2.—Patient placed lying down on the plate changer. Everything is ready for the injection.

The pathologic changes of the abdominal aorta and of the iliac arteries can be studied by retrograde arteriography. Atheroma is the most frequent lesion that I have encountered in these arteries. The characteristic picture produced by atheroma is due to loss of elasticity of the arteries leading to elongation and dilatation of the vessels, together with stenosis caused by lesions of the intima and secondary calcification. Atheroma is usually found in old age and the lesions are generally seen all along the vessels, being more prominent in the aortic cone and in the iliac arteries (Fig. 3).

Arteriography allows us to study any changes in contour present in both the aorta and iliac arteries clearly showing any strictures or dilatations present. Elongation of these vessels produces vascular kinking that leads to obliteration (Fig. 4). The size of the lumen of the artery and its course permits us to

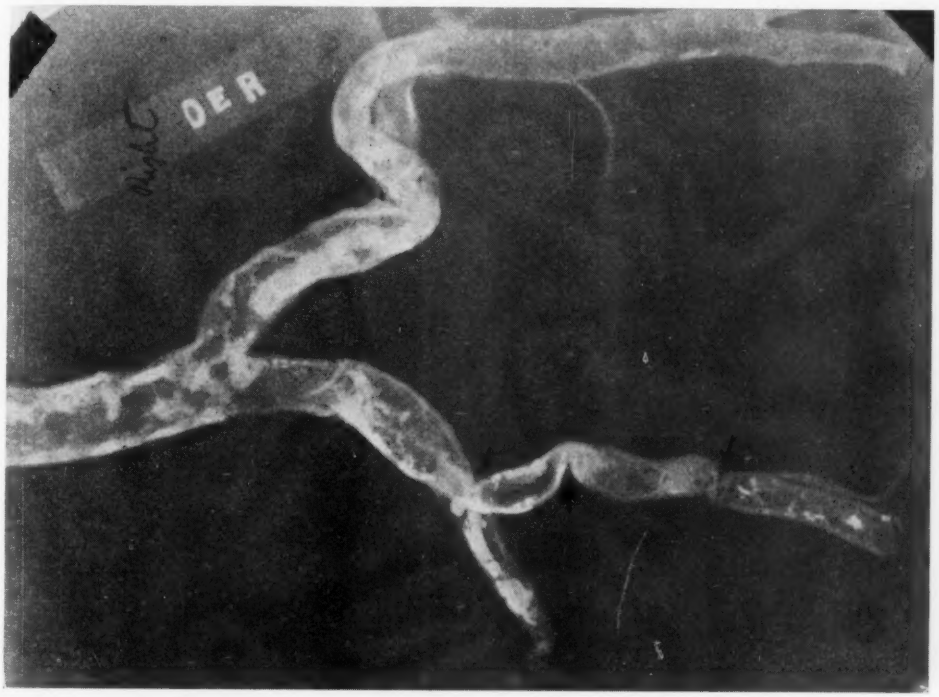

Fig. 4.

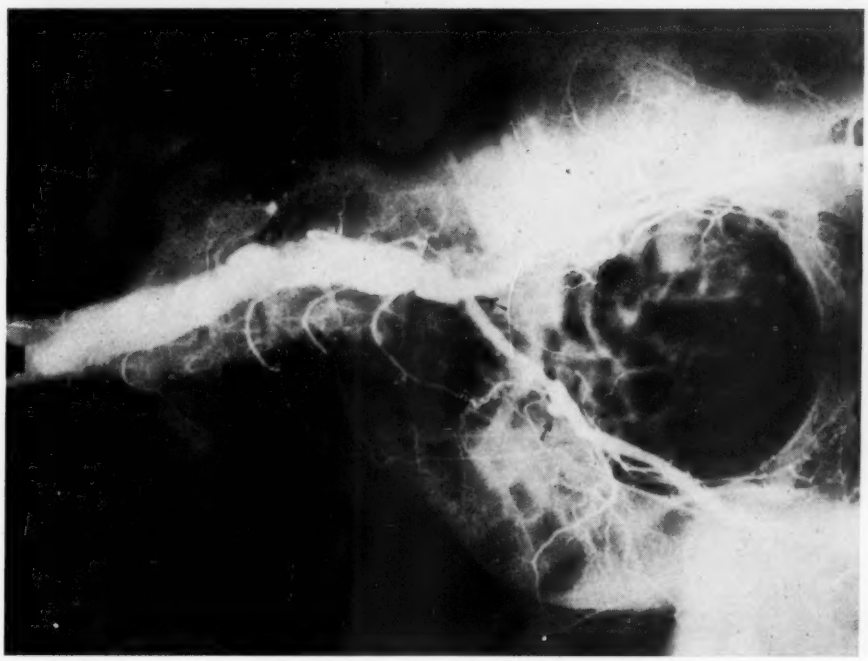

Fig. 3.

Fig. 3.—Advanced atheromatous degeneration of the aorta and iliac arteries. Notice the almost complete occlusion at the aortic cone and the aneurysms of the right iliac and left internal iliac arteries.

Fig. 4.—X-ray of the anatomic specimen showing the marked calcification and kinking of the arteries.

determine with great accuracy the actual degree of obstruction or calcification. In the presence of aneurysms of the abdominal aorta and iliac arteries, it is possible with this method to determine their localization, extension, the degree of permeability of the aneurysmal sac, the presence of canalization due to organization of blood clots, and the degree of collateral circulation (Figs. 5 and 6).

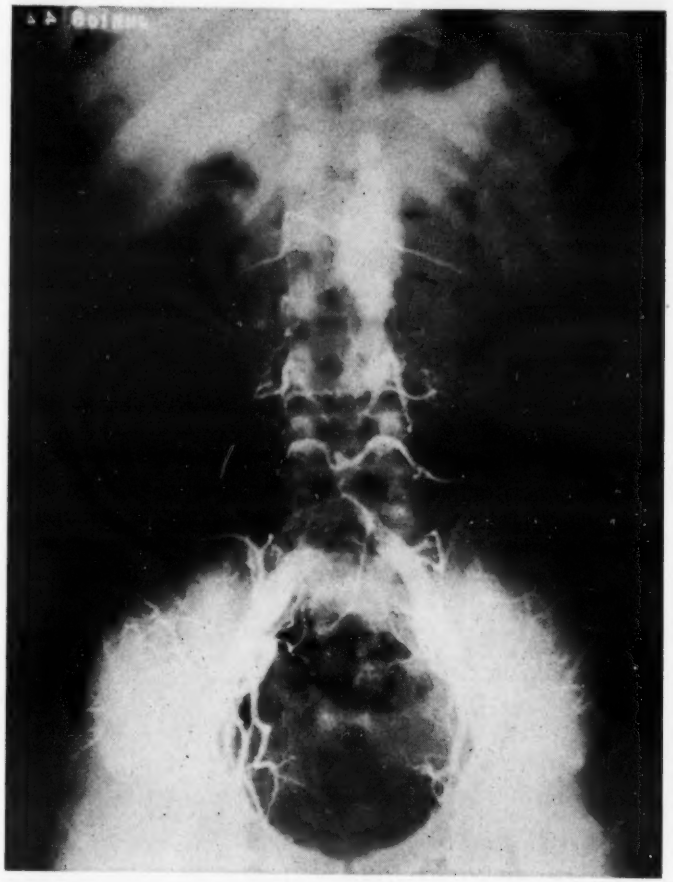

Fig. 5.

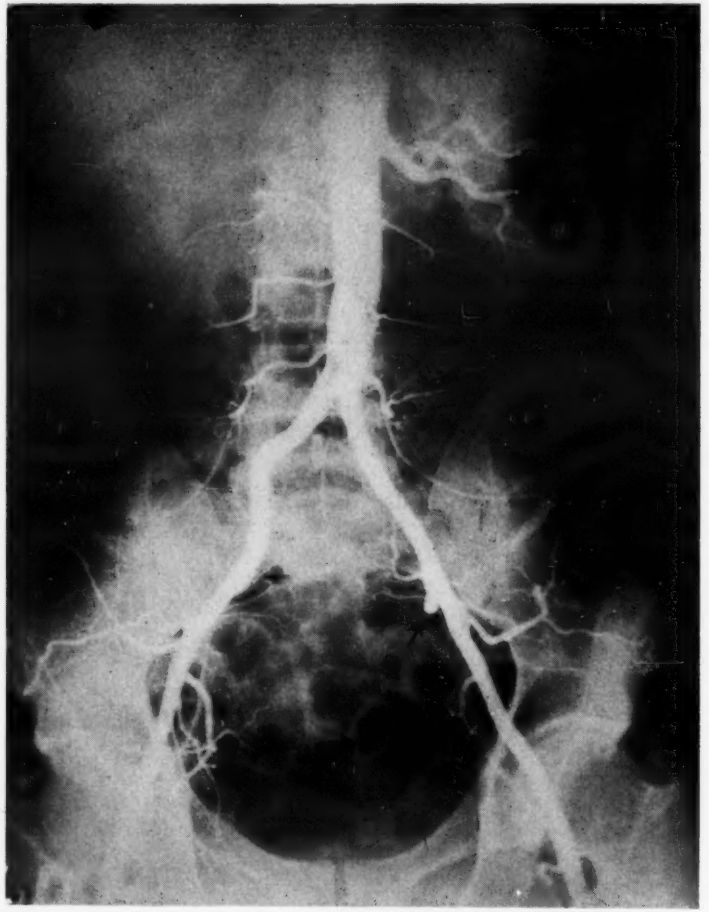

Fig. 6

Fig. 5.—Canalized aneurysm of the abdominal aorta. Ligation of both iliac arteries was practiced with marked reduction of aneurysm and complete subsidence of pain.

Fig. 6.—Aneurysm of the left iliac artery.

With this procedure we can also study the characteristics of collateral circulation in cases of complete obstruction of the aortic cone. This collateral circulation takes place by the double anastomosis of the internal mammary with the epigastric artery and the circumflex iliac with the lumbar arteries, thus providing the blood irrigation of the inferior limb.

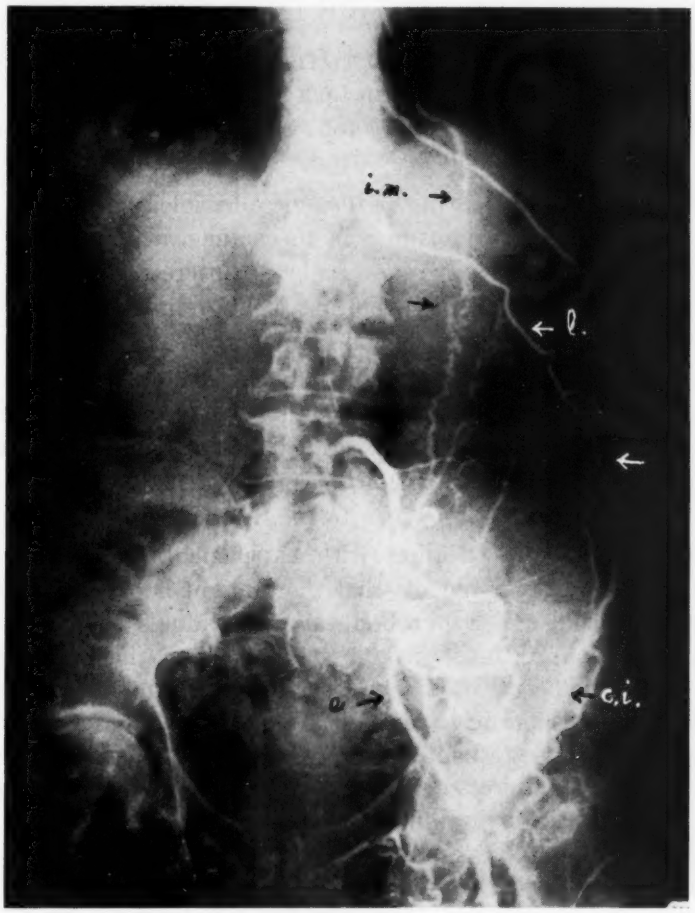

Fig. 7.—Complete obstruction of the cone of the aorta and iliac arteries due to advanced atheroma. Notice the two collateral arches; the internal, formed by the epigastric artery (*e*) and internal mamary (*i.m.*), and the external by the circumflex iliac (*c.i.*) and the lumbar arteries (*l*).

I have had no accidents with this method, even though I have used it in patients in very poor physical condition and with advanced arterial lesions.

The pathologic changes in the visceral branches of the abdominal aorta will be presented in another paper.

BODY FLUID AND PLASMA PROTEIN CHANGES FOLLOWING A SINGLE NONFATAL HEMORRHAGE IN HYPOPROTEINEMIC DOGS

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AN UNDERSTANDING of the pathologic physiology resulting from acute blood loss is of great importance in the management of medical and surgical patients. During recent years renewed interest has become manifest in this subject. In the past the attention of the clinician has been directed principally at the restoration of blood cells and hemoglobin following acute hemorrhage. However, recent studies indicate that restoration of plasma volume and restoration of total circulating plasma proteins are equally if not more important phenomena since these processes help to re-establish the hemodynamics of the peripheral circulation so that any hemoglobin that may remain can carry out its function of transporting oxygen to the tissues.

The results of studies dealing with experimental hypoproteinemia and plasma protein regeneration suggest that there might be a marked difference in the recovery of normal and hypoproteinemic individuals from an acute hemorrhage. Thus, if attention is limited to the changes of the plasma volume and the plasma protein concentration which have been found to occur following a single nonfatal hemorrhage in normal dogs[1-8] and man,[9, 10] it would appear that there is a prompt, but gradual, inflow of fluid and plasma protein into the circulation. The initial increase of plasma volume is apparently the result of the addition of fluid relatively low in protein and in from several hours to some seventy hours the plasma volume may be found to exceed the control level. In general, it has been found that the plasma protein (albumin) is restored more slowly than the plasma volume and may still be incomplete at the end of several days. Since there is evidence[10] that after hemorrhage the blood volume is not restored to normal until new plasma protein has been added to the circulation, the present study was carried out in order to compare the spontaneous recovery of normal and hypoproteinemic animals from a single severe nonfatal hemorrhage.

METHODS AND CALCULATIONS

Young adult dogs were used in this study and were placed on a constant diet* for at least seven days before the experiments were undertaken. Hypoproteinemia was then induced in one group of animals by feeding a diet low in protein for a period of four weeks.

The animals were bled 25 per cent of the measured blood volume (estimated from the plasma volume and the hematocrit) without anesthesia, by direct puncture of the femoral artery. Food was withheld for the previous 24 hours and no food or water was allowed for 24 hours after the hemorrhage. After the 24-hour period the animals were again given the respective diets received

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*Purina Dog Chow, Purina Mills, St. Louis, Mo.

before the hemorrhage. One group of the normal and hypoproteinemic dogs was studied before and 4 hours after the hemorrhage. A second group of dogs was studied before and 24 hours after the bleeding. Both groups of dogs were then studied again from 96 to 120 hours after the hemorrhage.

The following determinations were carried out in the control and experimental periods: the plasma volume, the "available (thiocyanate) volume," the total plasma protein and plasma albumin concentrations, and the hematocrit. The methods of determination were the same as those employed in a previous paper.[11]

The total circulating plasma protein and total circulating plasma albumin were calculated by multiplying the plasma volume in cubic centimeters by the grams of protein per cubic centimeter. The amounts of total plasma protein and plasma albumin removed from the circulation by the bleeding and by the withdrawal of blood for the chemical determinations were estimated by multiplying the volume of plasma withdrawn (c.c. whole blood withdrawn $\times \frac{100 - \text{hematocrit}}{100}$) in cubic centimeters by the grams of plasma protein or plasma albumin per cubic centimeter. The amounts of total plasma protein and plasma albumin restored during the given test period were obtained by deducting from the grams of total plasma protein and plasma albumin removed, the differences of the measured amounts (control and experimental values) of total circulating plasma protein and total circulating plasma albumin, respectively.

EXPERIMENTAL

The average blood changes which were encountered in normal and hypoproteinemic dogs in 4 hours, 24 hours, and in 96 to 120 hours following a single nonfatal hemorrhage have been presented in Tables I to III.

Changes of the Plasma Volume and "Available (Thiocyanate) Volume."— From the data presented in Table I it will be seen that in normal dogs 4 hours following a loss of blood amounting to 25 per cent of the control blood volume, there were decreases of the average plasma volume and "available (thiocyanate) volume" levels. In 24 hours after the bleeding (Table II) the average plasma volume was found to approach the average control level while the average "available (thiocyanate) volume" remained reduced. When the animals were allowed food and water following the 24-hour period and observed again in

TABLE I. AVERAGE BLOOD CHANGES FOUR HOURS AFTER A SINGLE NONFATAL HEMORRHAGE IN NORMAL AND HYPOPROTEINEMIC DOGS*

	NORMAL DOGS (4)		HYPOPROTEINEMIC DOGS (3)	
	CONTROL	4 HOURS	CONTROL	4 HOURS
Body weight (kg.)	12.3		9.2	
Plasma withdrawn (c.c.)	151		130	
Hematocrit (per cent)	40.8	34.9	38.0	33.7
Plasma volume (c.c.)	565	505	492	441
Thiocyanate volume (c.c.)	3,730	3,590	3,620	3,150
Total plasma protein (Gm. per 100 c.c.)	6.17	5.46	4.31	3.81
Plasma albumin (Gm. per 100 c.c.)	3.49	3.15	2.07	1.90
Total circulating plasma protein (Gm.)	34.9	27.8	21.3	16.9
Circulating plasma albumin (Gm.)	19.6	15.7	10.2	8.5
Total plasma protein removed (Gm.)	9.4		5.6	
Total plasma albumin removed (Gm.)	5.3		2.7	
Total plasma protein restored (Gm.)†		2.3		1.2
Plasma albumin restored (Gm.)†		1.4		1.0

*Twenty-five per cent of the measured blood volume drawn. The numbers within the parentheses indicate the number of animals.

†The values were obtained by deducting from the grams of total plasma protein and albumin removed the differences of the measured amounts of total circulating plasma protein and total circulating plasma albumin, respectively.

TABLE II. AVERAGE BLOOD CHANGES TWENTY-FOUR HOURS AFTER A SINGLE NONFATAL HEMORRHAGE IN NORMAL AND HYPOPROTEINEMIC DOGS*

	NORMAL DOGS (4)		HYPOPROTEINEMIC DOGS (3)	
	CONTROL	24 HOURS	CONTROL	24 HOURS
Body weight (kg.)	12.5	11.8	11.4	10.3
Plasma withdrawn (c.c.)	144		144	
Hematocrit (per cent)	43.9	35.2	37.9	31.6
Plasma volume (c.c.)	546	538	550	515
Thiocyanate volume (c.c.)	3,660	3,460	3,820	3,470
Total plasma protein (Gm. per 100 c.c.)	5.91	5.51	4.37	4.02
Plasma albumin (Gm. per 100 c.c.)	3.17	3.09	1.81	1.70
Total circulating plasma protein (Gm.)	32.1	30.0	24.4	20.7
Circulating plasma albumin (Gm.)	17.0	16.3	10.0	8.8
Total plasma protein removed (Gm.)	8.5		6.3	
Total plasma albumin removed (Gm.)	4.6		2.6	
Total plasma protein restored (Gm.) †		6.3		2.7
Plasma albumin restored (Gm.) †		3.8		1.4

*See footnote to Table I.
†See footnote to Table I.

from 96 to 120 hours after the hemorrhage, the average plasma volume and "available (thiocyanate) volume" levels (Table III) were found to be in excess of the average control values.

It will be noted that following a nonfatal hemorrhage in normal dogs the restoration of the plasma volume apparently proceeds promptly. At the end of 4 hours (Table I) the fluid entering the circulation represented, on the average, 60 per cent and at the end of 24 hours (Table II), 94 per cent of the plasma withdrawn. Since no fluid replacement (orally or by vein) was instituted during the latter periods, the fluid entering the circulation represented a redistribution of body water. Although a true evaluation of the changes of the "available (thiocyanate) volume" is difficult, the direction of the changes supports the belief that the fluid entering the plasma was derived chiefly from the interstitial spaces.

The changes of the plasma volume and "available (thiocyanate) volume" which were encountered following the hemorrhage in the hypoproteinemic animals are of considerable interest. As in the normal dogs treated in the same manner, there was evidence of an equally prompt but gradual addition of fluid to the plasma, which was associated with a fall of the "available (thiocyanate) volume" level. Thus, at the end of 4 hours (Table I) the fluid entering the circulation represented, on the average, about 60 per cent and at the end of 24 hours (Table II), 76 per cent of the plasma withdrawn. Observations which were made 96 to 120 hours after hemorrhage (Table III) revealed that the average plasma volume and "available (thiocyanate) volume" levels had returned to the respective average control values.

Changes of the Plasma Protein Concentration and the Hematocrit.—From a perusal of the data presented in the tables it will be noted that there were some similarities in the two groups of animals with respect to the directions of the average changes of the total plasma protein and plasma albumin concentrations and the hematocrit. Thus, in both the normal and the hypoproteinemic animals, decreases of the average values for the total plasma protein and plasma albumin concentrations and the hematocrit were obtained 4 hours and 24 hours following the hemorrhage (Tables I and II). Further, deficits of these constituents from the average control levels still persisted 96 to 120 hours after the hemorrhage (Table III). If the percentage changes from the respective control levels are considered, it will be found that the per cent deficit of the average hematocrit was greater than the per cent deficits for the total plasma protein

TABLE III. AVERAGE BLOOD CHANGES 96 TO 120 HOURS AFTER A SINGLE NONFATAL HEMORRHAGE IN NORMAL AND HYPOPROTEINEMIC DOGS*

	NORMAL DOGS (6)		HYPOPROTEINEMIC DOGS (6)	
	CONTROL	AFTER 96-120 HOURS	CONTROL	AFTER 96-120 HOURS
Body weight (kg.)	12.3	12.0	10.3	9.9
Plasma withdrawn (c.c.)	176		163	
Hematocrit (per cent)	41.8	32.6	37.9	29.0
Plasma volume (c.c.)	568	631	521	539
Thiocyanate volume (c.c.)	3,740	3,900	3,720	3,730
Total plasma protein (Gm. per 100 c.c.)	6.01	5.61	4.34	3.99
Plasma albumin (Gm. per 100 c.c.)	3.24	3.10	1.94	1.75
Total circulating plasma protein (Gm.)	34.1	35.5	22.9	21.7
Circulating plasma albumin (Gm.)	18.3	19.5	10.1	9.4
Total plasma protein removed (Gm.)	10.6		7.1	
Total plasma albumin removed (Gm.)	5.7		3.2	
Total plasma protein restored (Gm.)†		11.8		5.8
Plasma albumin restored (Gm.)†		7.0		2.5

*See footnote to Table I.
†See footnote to Table I.

and plasma albumin concentrations. This observation can be taken to indicate that some protein had entered the plasma during the period of observation. In addition, the per cent fall of the average hematocrit was found to be the lowest at 4 hours after the hemorrhage and the greatest at the end of the 96- to 120-hour period. On the basis of the hematocrit change, therefore, it can be inferred that there was a progressive blood dilution during the period of observation, which supports the findings for the plasma volume previously noted.

Plasma Protein Regeneration.—The differences between the measured amounts of total circulating plasma protein on the one hand and total circulating plasma albumin on the other, deducted from the respective amounts of total plasma protein and plasma albumin removed as the result of the bleeding, were taken to represent the amounts of total protein and albumin which had entered the plasma during the given test periods. Thus, from the data presented in Table I it will be seen that with the bleeding of the normal dogs, an average of 9.4 Gm. of total plasma protein and an average of 5.3 Gm. of plasma albumin were removed. Further, in 4 hours after the hemorrhage, on the average, 2.3 Gm. of total protein and 1.4 Gm. of albumin had been added to the plasma. In other words, about 24 per cent of the average total plasma protein and about 26 per cent of the average albumin removed from the plasma as the result of the hemorrhage were restored in 4 hours. Similarly, in 24 hours after the hemorrhage (Table II) normal dogs were found to have added an average of 6.3 Gm. of total protein (about 74 per cent of the total protein removed) and an average of 3.8 Gm. of albumin (about 83 per cent of the albumin removed) to the plasma. When the observations were carried out 96 to 120 hours after the hemorrhage (Table III), and the animals allowed a normal diet beginning at the end of the 24-hour period, the amounts of total protein and albumin added to the plasma were found to exceed the amounts removed by the bleeding.

A similar analysis of the data obtained on the hypoproteinemic animals revealed that even in the presence of body protein depletion some protein entered the plasma following a single nonfatal hemorrhage. Thus, from Table I it will be seen that in 4 hours after the hemorrhage, on the average, 1.2 Gm. of total protein and 1.0 Gm. of albumin had been added to the plasma. These figures represented a restoration of about 21 and 37 per cent, respectively, of the total plasma protein and plasma albumin removed by the bleeding. Similarly, in 24 hours after the hemorrhage (Table II) the hypoproteinemic animals were

found to have added, on the average, 2.7 Gm. of total protein (representing about 43 per cent of the total protein removed) and 1.4 Gm. of albumin (amounting to about 54 per cent of the albumin removed) to the plasma. When the animals were again allowed the low protein diet at the end of the 24-hour period and the observations repeated 96 to 120 hours after the hemorrhage (Table III) it was found that some additional protein had entered the plasma. Thus, it will be seen that during the period, on the average, 5.8 Gm. of total protein (about 82 per cent of the total plasma protein removed) and 2.5 Gm. of albumin (about 78 per cent of the albumin removed) had been added to the plasma.

DISCUSSION

The data herein reported offer further support to the findings of other workers[1-8] that following a single nonfatal hemorrhage in normal dogs there is a prompt, but gradual, restoration of the plasma volume and of the total amount of circulating plasma protein. In the present experiments no nitrogen or fluid replacement (orally or intravenously) was instituted for a period of 24 hours after the hemorrhage. During a 4-hour interval in normal dogs the plasma was found to have regained, on the average, 60 per cent of the volume, 24 per cent of the total plasma protein, and 26 per cent of the plasma albumin lost by hemorrhage. Similarly, during a 24-hour period the plasma was found to have regained 94 per cent of the volume, 74 per cent of the total plasma protein, and 83 per cent of the plasma albumin lost by the bleeding. These figures support the view that the initial increase in plasma volume is due to the addition of fluid relatively low in protein and that albumin and globulin are restored at approximately the same rate. It should be pointed out that under similar experimental conditions, Fine, Fischmann, and Frank[7] found in a 4-hour period normal dogs regained, on the average, 53 per cent of the plasma volume and 30 per cent of the plasma protein lost by hemorrhage.

The data obtained with the hypoproteinemic animals, which were studied in identically the same manner as the normal dogs, are of some interest. Apparently, despite a state of protein depletion as evidenced by the reduced control plasma albumin concentration, the plasma regained during a 4-hour period, on the average, 60 per cent of the volume, 21 per cent of the total protein, and 37 per cent of the albumin lost by the hemorrhage. During a 24-hour period, the plasma regained, on the average, 76 per cent of the volume, 43 per cent of the total protein, and 54 per cent of the albumin lost. Whereas, on the average, the plasma volume was completely restored during a succeeding period of several days when the animals were allowed the low protein diet, the plasma protein restoration remained incomplete. The source of the protein which apparently was added to the plasma is not clear, since in these animals the stores of ready available protein were presumably depleted.

SUMMARY

Determinations of the plasma volume, "available (thiocyanate) volume," total plasma protein and plasma albumin concentrations, and hematocrit were carried out in normal and hypoproteinemic dogs before and following a single nonfatal hemorrhage (25 per cent of the measured blood volume). No nitrogen or fluid replacement was instituted for a period of 24 hours after the hemorrhage. The pertinent findings may be briefly summarized as follows:

1. Following a single nonfatal hemorrhage in normal dogs there was found to be a prompt, but gradual, restoration of the plasma volume and of the total amount of circulating plasma proteins. After the animals had resumed a

normal diet for several days the average levels for the plasma volume and the total circulating plasma proteins were found to exceed the average control values.

2. In normal dogs the initial increase in plasma volume was found to be due to the addition of fluid relatively low in protein. During a 4-hour interval, the plasma was found to have regained, on the average, 60 per cent of the volume, 24 per cent of the total protein, and 26 per cent of the albumin lost by the hemorrhage.

3. The initial increase of plasma volume following hemorrhage was found to be associated with a fall of the "available (thiocyanate) volume." The direction of these changes, when no fluid replacement was instituted, was taken to indicate that the fluid entering the plasma was derived chiefly from the interstitial spaces.

4. The plasma volume was found to increase promptly following a single nonfatal hemorrhage in hypoproteinemic dogs. Observations which were made 4 hours and 24 hours after the hemorrhage indicated that some protein had been added to the plasma. Even though the average plasma volume returned to the control level, after the animals had resumed a low protein diet for several days, plasma protein restoration was incomplete.

5. Despite the fact that the animals were in a state of protein depletion, the plasma regained during a 4-hour period, on the average, 60 per cent of the volume, 21 per cent of the total protein, and 37 per cent of the albumin lost by the hemorrhage. The source of this protein was not apparent.

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INTERSCAPULOTHORACIC DISARTICULATION OF THE ARM

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INTERSCAPULOTHORACIC disarticulation is a term used to denote the removal of the entire arm and shoulder. This includes the scapula, the outer two-thirds of the clavicle, and all attached muscles and fasciae.

The operation was first done by Ralph Cumming of the Royal Navy in 1808. Dixie Crosby of New Hampshire introduced it in America in 1836. Paul Berger of France wrote an exhaustive monograph on the subject in 1887 and gave the operation its present name. The older books of surgery describe it accurately; however, modern texts devote very little space to it, because they aver it is too radical and is rarely indicated. It is our purpose in this paper to define the indications for the procedure, to describe its technique, and to call attention to the importance of this old operation under modern diagnostic and surgical methods.

According to Pack and associates there were twenty-nine recorded interscapulothoracic amputations until 1881, the pre-Listerian era, with an operative mortality of 38 per cent. Berger reduced this to 10.4 per cent. Buchanan analyzed the 141 reported operations up to 1900. Pack and his associates studied an additional 180 reported cases and added 31 of their own. We therefore have a record of 381 patients upon whom the operation has been performed to date. Undoubtedly this is but a small fraction of the actual number done. In Buchanan's group the mortality of the operation was 11.3 per cent. In the collected series of Pack and his co-workers it was 5 per cent and in their own 31 cases there was none. We are reporting an additional 5 cases without operative mortality. In tabulating our findings we have followed the outline suggested in previous studies so that pertinent data may be assembled in a uniform manner.

INDICATIONS FOR THE OPERATION

Interscapulothoracic disarticulation is indicated in the treatment of the following conditions:

Soft tissues

1. All carcinomas of the hand or forearm or arm with metastases to the axilla as determined by lymph node biopsy

2. All proved carcinomas of the arm involving the humerus or shoulder joint, or any of the shoulder muscles

3. Axillary tumors adherent to the vessels and nerves, which cannot be excised locally

4. Extensive trauma which is irreparable

5. Large ulcerating, infected, and painful axillary growths even though metastases are present; pain alone in neoplasms with metastases not an indication; can be remedied by chordotomy or posterior rhizotomy

Presented at the Fifty-Second Annual Meeting of the Western Surgical Association, Chicago, Ill., Dec. 1 and 2, 1944.

Bone

1. Sarcomas of the humerus clavicle or scapula
2. Usually though not invariably sarcoma of the forearm

Most patients included in these groups have had local excisions or less radical amputations. It would be well to consider this procedure as the treatment of choice at the outset. This would greatly enhance its curative possibilities.

MERITS OF THE OPERATION

The operation is well conceived. It permits a correct anatomic approach and a complete excision of the morbid anatomy. The blood supply is controlled first. This is a fundamental principle in any extirpative procedure because it reduces operative bleeding. Moreover, in this instance it prevents blood stream dissemination which may result from the loosening of neoplastic cells which have invaded the veins. For this reason we clamp the artery, then tie the vein without raising the arm to empty it of blood. Littlewood's method of interscapulothoracic disarticulation is by a posterior approach. It may be useful in very obese patients or in those with large tumors in front.

The disarticulation permits the complete excision of all anatomic lymphatics and lymph nodes, all related muscular and fascial planes, and all involved axillary tissue, together with the related bones. This may be done as a unit operation with less blood loss than in a radical mastectomy. The skin flaps are usually adequate so that skin grafts are ordinarily unnecessary.

The mortality rate of this radical operation is no greater than for ordinary amputations of the upper arm. Therefore, aside from the disfigurement and inconvenience produced, there are no objections to its use. Certainly these are inconsequential objections, when compared with the additional chances for cure. If a portion of the arm must be removed, then the inconvenience is not much greater and the disfigurement, though unsightly, may be rectified by proper shoulder pads.

TECHNIQUE

Our method is essentially that of Berger with slight modifications of various authors, including our own.

Ether anesthesia by the open-drop method is employed. The patient is placed on the edge of the table with sandbags under the ipsolateral vertebral margin. The arm, chest, neck, and back are surgically prepared and the forearm is covered with sterile towels which are held by a sterile bandage so that the extremity may be moved in any direction.

The primary incision is made parallel with and directly over the clavicle (Fig. 1). The sternocleidomastoid muscle is partially divided from its clavicular origin and the lateral two-thirds of the clavicle are subperiosteally resected. (Berger suggested the middle third, Le Conte the entire clavicle.) By inserting the finger beneath the pectoralis major, the operator may safely separate this muscle from its clavicular attachment. Here the cephalic vein is tied and divided. The subclavius muscle and the overlying periosteum are divided transversely in line with the medial edge of the divided clavicle and reflected laterally (Fig. 2). The anterior incision is carried downward medial to the coracoid process (Kocher). Care must be taken not to injure the dome of the pleura on either side and the thoracic duct on the left.

With this exposure the vascular supply may be clearly identified and controlled. The transverse scapular and transverse cervical veins are tied and

divided before their junction with the external jugular. Next the transverse scapular (suprascapular) artery, a branch of the thyrocervical trunk, is divided between ligatures. It lies anterior to the subclavian artery and is separated from it by a process of the deep cervical fascia which binds the tendon of the posterior belly of the omohyoid muscle to the scapula and first rib.

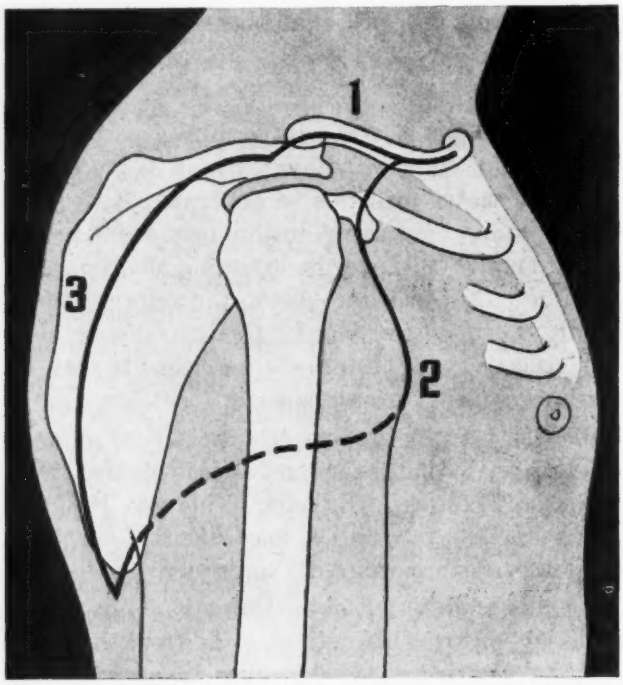


Fig. 1.—Lines of incisions for interscapulothoracic disarticulation. The numbers indicate the order in which the dissections are made.

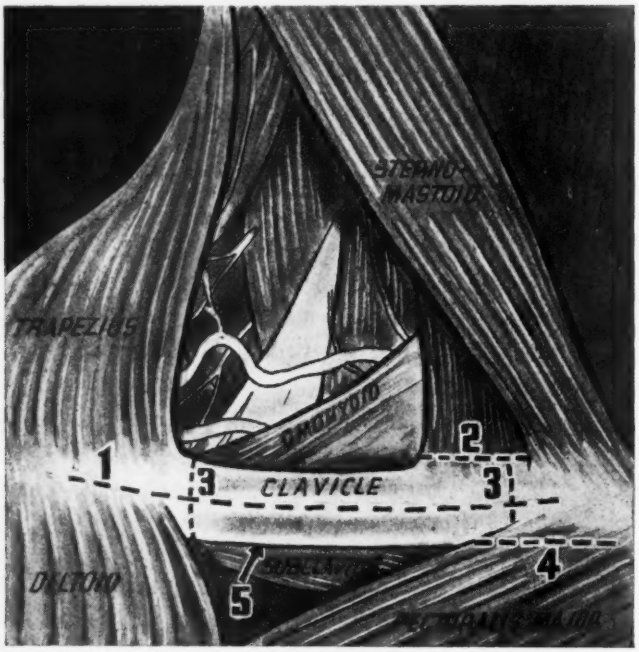


Fig. 2.—Diagram illustrating the anatomy of the subcutaneous structures. *1*, Incision in the periosteum of the clavicle; *2*, division of sternomastoid muscle from its clavicular origin; *3*, subpereosteal removal of the lateral two-thirds of the clavicle; *4*, separation of the pectoralis major muscle from the clavicle; *5*, severance and lateral reflection of the subclavius and its overlying periosteum in line with medial edge of divided clavicle.

When this muscle is traced upward, the transverse cervical artery (another branch of the thyrocervical trunk) is encountered medial to this muscle. It is tied and divided. The artery usually divides into an ascending (superficial cervical) and descending (posterior scapular) branch when it reaches the anterior border of the trapezius. Occasionally the ascending branch arises from the thyrocervical trunk whereas the descending branch comes directly from the third portion of the subclavian. In this case the former is called the superficial cervical artery, whereas the latter is termed the transverse cervical artery. It is this branch which is divided between ligatures in such anomalies (Fig. 3).

The subclavian vein lies anterior and slightly inferior to the artery. It is carefully dissected loose from the artery, which is clamped. The vein is triply tied with heavy silk and divided between the two lateral transfixed ligatures (Fig. 4). The artery is then tied with a simple ligature. Lateral to this, two transfixed ties are introduced and the vessel is divided between them.

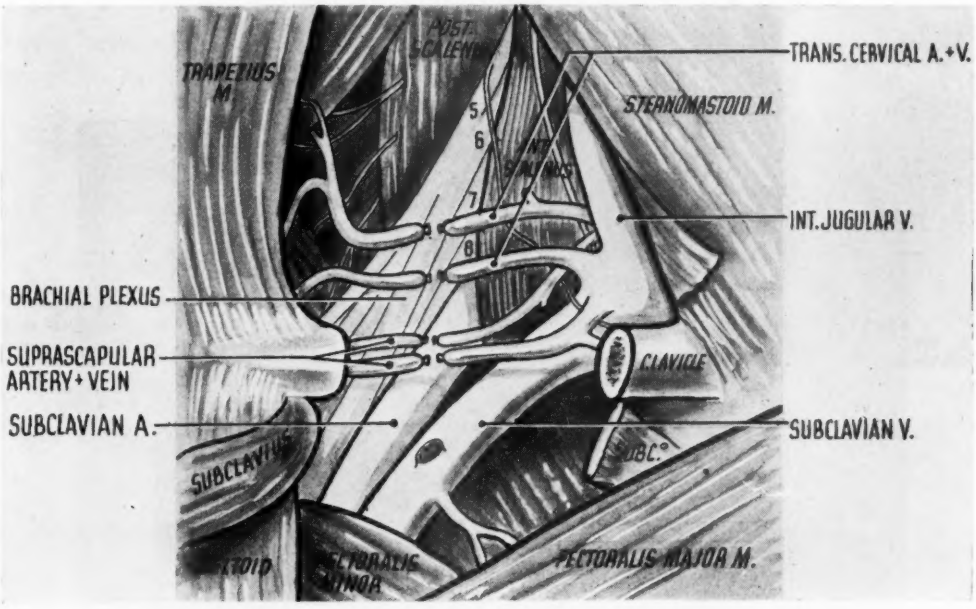


Fig. 3.—Diagram of the deep anatomy. The transverse cervical and transverse scapular arteries and veins have been divided between ligatures.

Up to this point the arm has not been moved because of the possibility of dislodging malignant cells by the manipulation. It is usually recommended that the arm should be elevated and all blood drained. We feel that it is better to lose the small amount of retained blood than to risk the dislodgment of neoplastic cells.

The anterior incision is carried downward along the pectorodeltoid groove to the upper axilla where it is continued posteriorly. The skin flaps are mobilized and the pectoralis major and minor and serratus anterior muscles are divided from their attachments to the ribs. The nerves of the brachial plexus are tied and divided with a sharp knife. They are not injected with 95 per cent alcohol. We have found that the incidence of amputation neuroma is not reduced by this procedure and phantom pain is more apt to occur.

The arm is now held across the body and the posterior incision is made along the borders of the scapula. The muscles divided beginning above the acromion process are the trapezius, omohyoid, levator scapulae, rhomboideus

minor and major, and latissimus dorsi. The teres major and minor, subscapularis, supra- and infraspinatus are removed with the arm (Fig. 5).

Skin flaps are brought together without tension. One small Penrose drain is inserted through a stab wound in the dependent flap. All of our wounds have healed per primam.

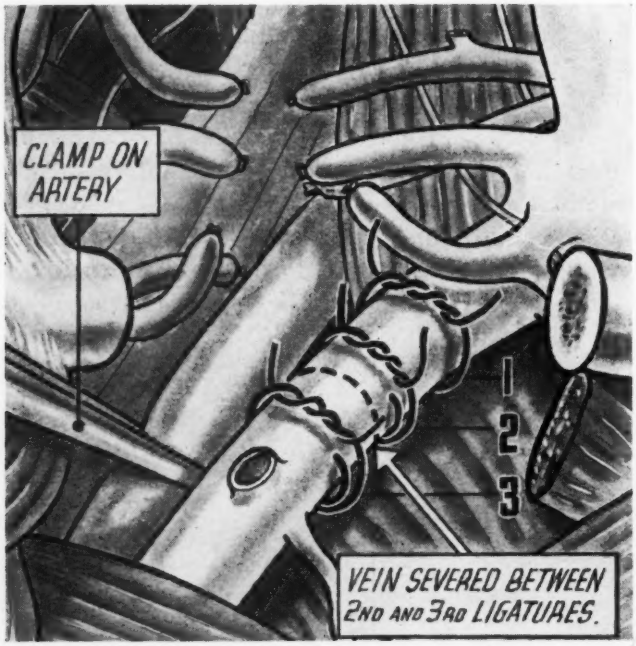


Fig. 4.—Method of vascular control; the subclavian artery has been clamped, the vein is tied with large silk ligatures. *1*, A simple tie; *2* and *3*, transfixed ligatures. The subclavian artery is then handled in a similar manner.

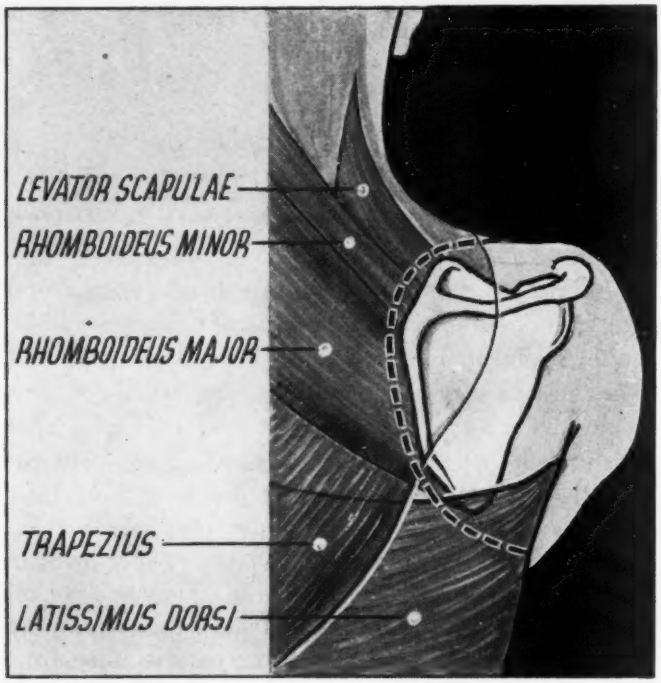


Fig. 5.—Line of posterior incision. The arm has been moved across the chest displacing the scapula laterally.

Blood loss in this procedure is surprisingly small. The operation is well borne with a minimum degree of shock. Patients may sit up in bed within twelve hours and in a chair in twenty-four hours.

COMPLICATIONS AND SEQUELAE

Hemorrhage may occur due to tearing of the vein at operation, slipping of a ligature, or erosion by a malignancy which when removed leaves a hole or a devitalized area in the vessels. We have not encountered such complications. Pack and his associates reported a case in which the subclavian vein was accidentally opened and air audibly aspirated into the vein. Hemorrhage was great but was controlled by compressing the vein with a finger against the first rib. The patient developed the symptoms of shock; he was given a blood transfusion and recovered. The danger of air embolism is real, but is probably exaggerated except in the pulmonary veins. In this instance the bolus of air is carried directly to the left heart where it may easily be sent to the brain, producing an immediate fatality. In the rest of the venous system the air is carried to the lungs where it is less apt to cause serious effects although these have been reported. It must require a large amount of air or a peculiar set of circumstances to produce any alarming results.

Fig. 6.—Clinical photograph (J. B.) showing large carcinoma of right hand. There had been previous attempts at removal. Axillary metastases were present.

Shock may result from the operation, but if the patient is properly prepared this should not occur even in old people.

"Phantom limb" with slight pain was observed in one of our patients (W. C.) This persisted for fourteen months but has now disappeared. The pain was referred chiefly to the dorsum of the hand. This was the site of the large and painful carcinoma (Fig. 7). Amputation neuroma with severe pain occurred in another patient (B. S.). The divided nerves had been injected with 95 per cent alcohol after ligature. Pain persisted during the remainder of the patient's life, a period of twelve months. Since local injection of procaine into the neuroma did not benefit the patient, excision of the lesion was not attempted. These pains may be due to local irritation of end bulb neuromas or a projection from the sensory areas in the cerebral cortex. The best prophylaxis is, first and foremost, as little handling of the brachial plexus as possible. Second, division of the nerve trunks with a sharp scalpel at a high

TABLE I. INTERSCAPULOTHORACIC DISARTICULATION OF THE ARM

CASE	DATE OF OPERATION	AGE, SEX, COLOR	DURATION OF SYMPTOMS	PREVIOUS OPERATIONS	LOCATION OF PRIMARY LESION	METASTASES AT THE TIME OF OPERATION	HISTOLOGIC TYPE	TYPE OF OPERATION	X-RAY THERAPY		CAUSES OF DEATH		DURATION OF LIFE AFTER OPERATION	COMMENTS
									PREOPERATIVE	POSTOPERATIVE	METASTASES	RECURRENCE		
O. S.	6/ 5/39	12 yr., F, White	1 yr.	Biopsy osteosarcoma	L. humerus upper ⅓	None	Osteolytic osteogenic sarcoma	Berger	200 kv.	None	Lungs	No	7 mo.	Auto accident 2 yr. before
M. G.	10/29/41	15 yr., F, Negro	11 mo.	Biopsy fibrosarcoma	R. humerus upper ⅓	None	Osteolytic osteogenic sarcoma	Berger	200 kv.	200 kv.	Lungs, vertebrae, brain, right ovary	No	8 mo.	Post-mortem examination
B. S.	9/12/43	64 yr., M, White	3 yr.	Biopsy	R. axilla	None	Fibrosarcoma of right axilla	Berger; nerves injected	None	None	Brain, lungs, vertebrae	No	12 mo.	Severe pain in brachial plexus
J. B.	5/26/43	67 yr., M, White	1½ yr.	Biopsy hand and axillary nodes	R. hand	Extensive to axilla	Squamous-cell carcinoma of hand and axillary nodes grade III	Modified Kocher; no nerve injection	200 kv.	None	No	No	1 yr. 7 mo. alive and well	No phantom pain; no recurrence (See Fig. 6)
W. C.	6/ 9/43	74 yr., M, White	14 mo.	Biopsy of hand, epitrochlear and axillary nodes	L. hand	Extensive to epitrochlear and axillary nodes	Squamous-cell carcinoma of hand, epitrochlear, axillary nodes	Modified Kocher; no nerve injection	200 kv.	None	No	No	1 yr. 6 mo. alive and well	Phantom pain until 8/18/44, no pain now; no recurrence

level so that they will not be caught in the granulation tissue and scar of the wounds.

If "phantom limb" is due to the persistence of preoperative pain at the site of the primary growth, then early operation should be helpful. The cause of these pains is not definitely known and the large array of operative procedures offered for their cure is proof of this fact.

Fig. 7.—Clinical photograph (W. C.); recurrent carcinoma of left hand.

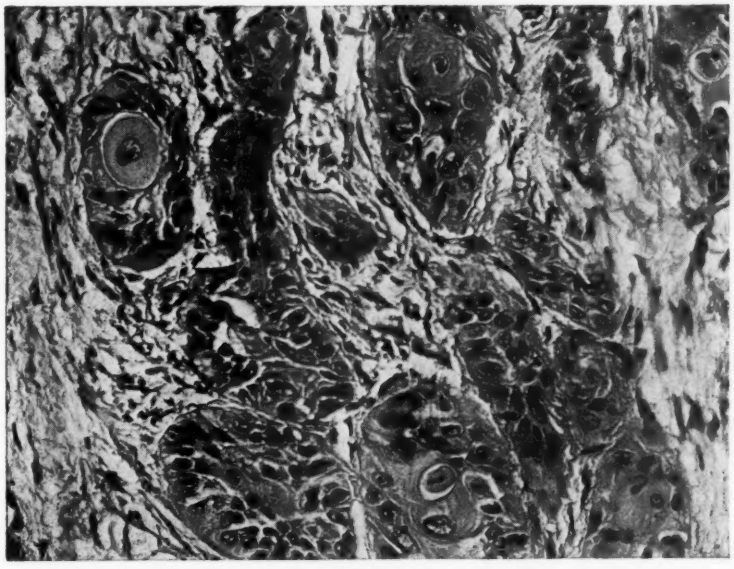
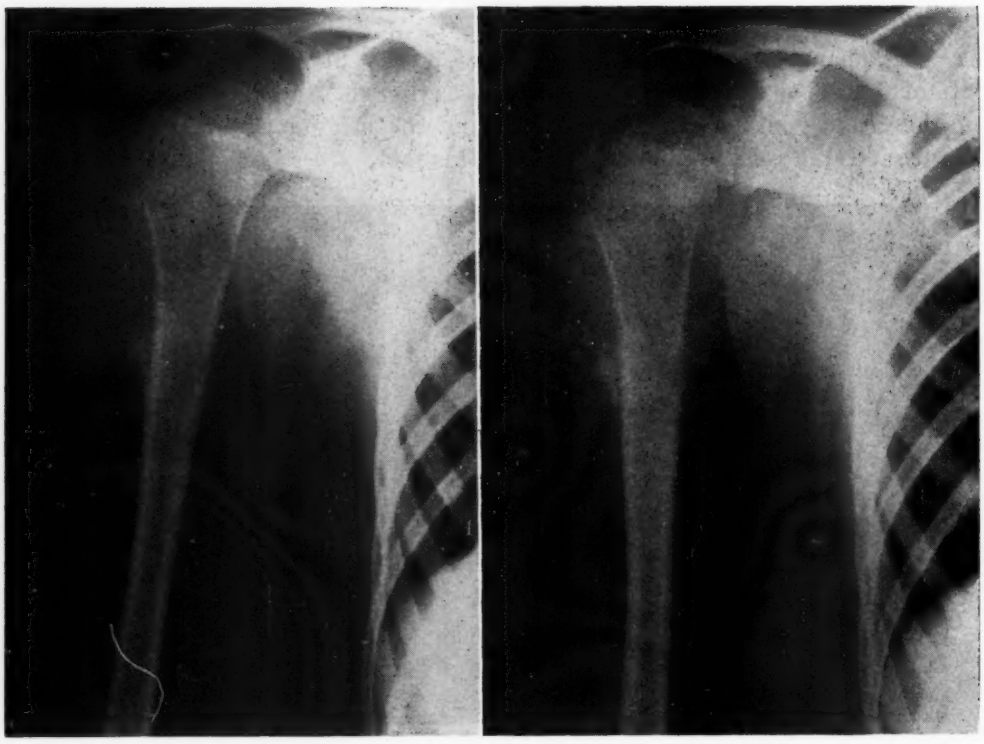


Fig. 8.—Axillary lymph node photomicrograph (W. C.); note complete replacement of lymphoid tissue by carcinoma cells and epithelial pearls.

RESULTS AND CONCLUSIONS

A summary of our cases is given in Table I. Our series is too small to draw any definite conclusions. It is also difficult to evaluate the larger series of Buchanan prior to 1900 because of possible errors in diagnosis.

The 31 cases reported by Pack and his associates are clearly presented. We feel that future studies should be summarized in like fashion so that accurate statistics may be gathered.



A. *B.*

Fig. 9.—X-ray photograph (O. S.) showing osteogenic osteolytic sarcoma of humerus. *A*, The bone destruction is clearly seen; *B*, soft tissue changes.

Fig. 10.—The disarticulated arm shown in Fig. 9.

From the experience of others and from our own observations we have drawn the following conclusions.

1. The operation may be safely done.

2. It may be done at any age. The youngest was 12, the oldest 74, average 48 years.

3. Soft tissue growths gave better results than lesions in bone. The former were in the older group and were carcinomas.

4. Symptoms were present from eleven months to three years. Average duration was fifteen and one-half months.

5. All patients had biopsies before operation. Four had one or more attempts at local extirpation.

6. Lymph nodes with metastases were present in the two cases of squamous-cell carcinoma. Metastases could not be demonstrated by x-ray in the cases of sarcoma at the time of operation (Fig. 7).

Fig. 11.—Clinical photograph (J. B.) showing scar ten days after operation. The wound has healed by first intention.

7. X-ray treatment was used preoperatively in four of our patients and postoperatively in one. The two surviving patients received preoperative x-ray therapy only. The value of this is unsettled although we feel that it should be used preoperatively with the idea that it may lessen the chance for metastasis and local recurrence. In radiosensitive or infected growths it may reduce their size, thereby facilitating complete extirpation.

8. None of our patients had local recurrences. The three deaths occurred from internal metastases. They were all patients with sarcoma.

9. The surviving patients are two men with squamous-cell carcinoma of the hand and axillary node metastasis, one, aged 67 years, alive and apparently

well nineteen months and the other, aged 74 years, alive and well eighteen months after the operation.

10. The end results of interscapulothoracic disarticulation are encouraging. Available statistics though meager prove that the operation offers a chance for cure in cases ordinarily considered hopeless.

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